=> □

=> d his ful

FILE 'REGISTRY' ENTERED AT 16:01:59 ON 12 JUL 2004

L14 STR

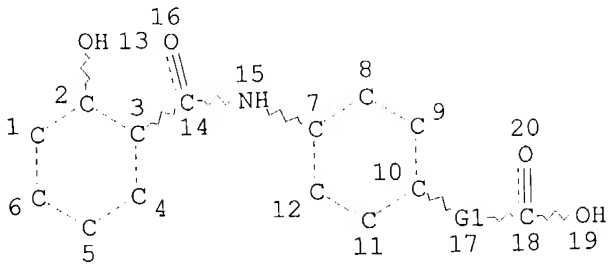
L15 5 SEA SSS SAM L14

L16 57 SEA SSS FUL L14 57 compds from Reg. - see I gave staff for structure

FILE 'HCAPLUS' ENTERED AT 16:05:58 ON 12 JUL 2004

L17 33 SEA ABB=ON L16 33 cits from CA Plus

=> d que stat l17
L14 STR



REP G1=(1-4) C
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 20

STEREO ATTRIBUTES: NONE
L16 57 SEA FILE=REGISTRY SSS FUL L14
L17 33 SEA FILE=HCAPLUS ABB=ON L16

=> d ibib abs hitstr l17 1-33

L17 ANSWER 1 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:696781 HCAPLUS
DOCUMENT NUMBER: 139:235382
TITLE: Method for administering GLP-1 molecules orally
INVENTOR(S): Khan, Mohammed Amin
PATENT ASSIGNEE(S): Eli Lilly and Company, USA; Jones, Bryan Edward; McGill, John McNeill
SOURCE: PCT Int. Appl., 72 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003072195	A2	20030904	WO 2003-US3111	20030207
WO 2003072195	A3	20040325		

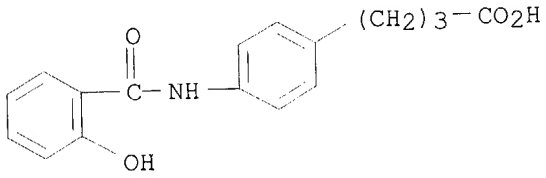
W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-358184P P 20020220

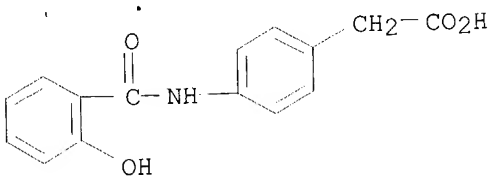
AB The invention encompasses formulations that demonstrate the feasibility of oral absorption comprising GLP-1 compds. and specified delivery agents.

IT **177653-18-8 590383-69-0**
RL: BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PKT (Pharmacokinetics); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(method for administering GLP-1 mols. orally)

RN 177653-18-8 HCAPLUS
CN Benzenebutanoic acid, 4-[(2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)



RN 590383-69-0 HCAPLUS
CN Benzeneacetic acid, 4-[(2-hydroxybenzoyl)amino]-, monosodium salt (9CI) (CA INDEX NAME)



● Na

L17 ANSWER 2 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:678792 HCAPLUS
DOCUMENT NUMBER: 139:214713
TITLE: Preparation of novel phenylalanine derivatives as α4 integrin inhibitors
INVENTOR(S): Sagi, Kazuyuki; Izawa, Hiroyuki; Chiba, Akira; Okuzumi, Tatsuya; Yoshimura, Toshihiko; Tanaka, Yuji; Ono, Miho; Murata, Masahiro
PATENT ASSIGNEE(S): Ajinomoto Co., Inc., Japan
SOURCE: PCT Int. Appl., 163 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003070709	A1	20030828	WO 2003-JP1852	20030220

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: JP 2002-43674 A 20020220
OTHER SOURCE(S): MARPAT 139:214713
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. [I; A = Q, Q1, Q2, Q3; wherein the ring Arm = cycloalkyl or aromatic ring containing 104 heteroatoms selected from O, S, and N; a solid line accompanied by a dotted line represents a single or double bond; U, V, X = CO, SO2, CR5R6, C(:CR5R6), C(S), S(O), P(O), P(O)OH, P(O)H; W = CR7, N; R1-R7 = H, halo, HO, lower alkyl, each (un)substituted lower alkyl, lower alkenyl, or lower alkynyl, aryl, heteroaryl, etc.; B = each (un)substituted lower alkoxy, NH2 (excluding NHOH), or SH; C = H, lower

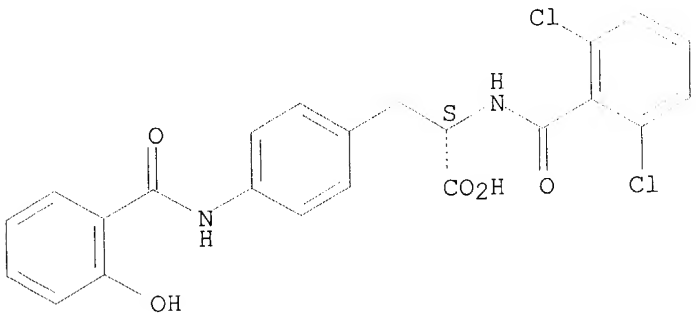
alkyl, lower alkenyl, lower alkynyl, cycloalkyl-lower alkyl (optionally containing a hetero atom in the ring), aryl-lower alkyl, heteroaryl-lower alkyl;D = lower alkyl, lower alkenyl, lower alkynyl, cycloalkyl, cycloalkyloxy, cycloalkyl-lower alkyl, or cycloalkyl-lower alkoxy each optionally containing a hetero atom in the cycloalkyl ring, aryl-lower alkyl, heteroaryl-lower alkyl, lower alkoxy, etc.; T = CO, C(S), S(O), SO2, NHCO, NHC(S); J, J1 = H, halo, lower alkyl, lower alkoxy, NO2] are prepared These phenylalanine derivs. I have an α4 integrin inhibitory effect and are useful as remedies for various diseases in which α4 integrin-dependent adhesion process participates, in particular inflammatory diseases, rheumatoid arthritis, inflammatory bowel diseases, systemic lupus erythematosus, multiple sclerosis, Sjogren syndrome, asthma, psoriasis, allergy, diabetes, cardiovascular diseases, arteriosclerosis, restenosis, tumor proliferation, tumor metastasis, or transplant rejection. Thus, (2S)-2-[(2,6-dichlorobenzoyl)amino]-3-[4-[6-(dimethylamino)-1-methyl-2,4-dioxo-1,4-tetrahydro-3(2H)-quinazolinyl]phenyl]propionic acid (II) (50 mg) (preparation by the solid phase method given), 26 μL Et3N, and 750 vL CH2Cl2 were added to a mixture of 1-chloroethyl cyclohexyl carbonate and 1-iodoethyl cyclohexyl carbonate (420 mg) and stirred at room temperature for 16 h, followed by distillation of the solvent and purification by reversed phase HPLC using aqueous acetonitrile containing 0.1% CF3CO2H as the mobile phase to give II 1-[(cyclohexyloxycarbonyl)oxy]ethyl ester trifluoroacetate which is a prodrug of II. II and (2S)-2-[(2-chloro-6-methylbenzoyl)amino]-3-[4-[1-methyl-2,4-dioxo-1,4-tetrahydro-3(2H)-quinazolinyl]phenyl]propionic acid inhibited the binding of recombinant human VCAM-1 to human T cell (Jurkat cell) known for expressing integrin α4β1 with IC50 of 57 and 34 nmol/L, resp., and that to human B cell lymphoma cell (RPMI-8866 cell) known for expressing integrin α4β7 with IC50 of 3.3 and 0.2 nmol/L, resp.

IT **401906-04-5DP**, Wang resin-bound
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of novel phenylalanine derivs. as α4 integrin inhibitors for treatment of diseases related to α4 integrin-dependent adhesion process)

RN 401906-04-5 HCAPLUS

CN L-Phenylalanine, N-(2,6-dichlorobenzoyl)-4-[(2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 3 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:695921 HCAPLUS
DOCUMENT NUMBER: 137:222089
TITLE: Compositions for delivery of bisphosphonates
INVENTOR(S): Boyd, Maria A. P.; Dinh, Steve
PATENT ASSIGNEE(S): Emisphere Technologies, Inc., USA
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002070438	A2	20020912	WO 2002-US6295	20020301
WO 2002070438	A3	20030424		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1372667	A2	20040102	EP 2002-723294	20020301

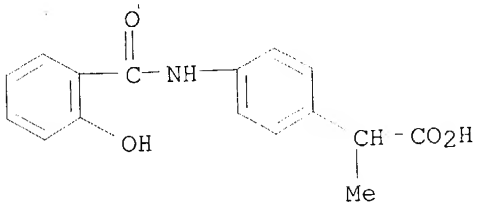
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

PRIORITY APPLN. INFO.: US 2001-272676P P 20010301
WO 2002-US6295 W 20020301

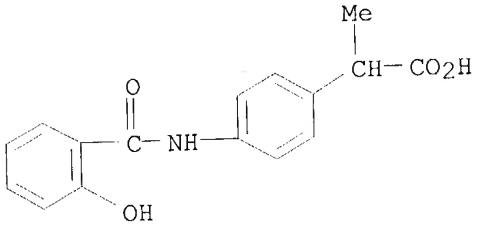
AB Compds. and compns. for the delivery of bisphosphonates are provided. Methods of preparation, administration and treatment are provided as well. Typically 400 mg of the delivery agent (sodium N-salicyloyl-8-aminocaprylate) was added to 2.0 mL of water. The solution was vortexed, then heated (about 37°) and sonicated. The pH was adjusted to about 7 with NaOH or HCl. Water was then added to bring the total volume to about 2.5 mL. Alendronate (25 μL) from a stock solution (made from 2.0 g sodium alendronate in 10 mL deionized water, pH adjusted to about 7.5 with 10 N NaOH, vortexed and sonicated at 37° to obtain a clear solution, frozen and defrosted before use) was added to the solution The final doses were 200 mg/kg delivery agent compound (i.e., 200 mg delivery agent/kg of body weight) and 2.5 mg/kg alendronate, and the volume dose was 1.0 mL/ kg.

IT **61126-76-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(compns. for delivery of bisphosphonates)

RN 61126-76-9 HCAPLUS
CN Benzeneacetic acid, 4-[(2-hydroxybenzoyl)amino]-α-methyl- (9CI) (CA INDEX NAME)



IT **257287-96-0P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(compns. for delivery of bisphosphonates)
RN 257287-96-0 HCAPLUS
CN Benzeneacetic acid, 4-[(2-hydroxybenzoyl)amino]-α-methyl-, monosodium salt (9CI) (CA INDEX NAME)



● Na

L17 ANSWER 4 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:157743 HCAPLUS
DOCUMENT NUMBER: 136:217047
TITLE: Preparation of novel phenylalanine derivatives having α4 integrin-inhibitory activity
INVENTOR(S): Makino, Shingo; Okuzumi, Tatsuya; Yoshimura, Toshihiko; Satake, Yuko; Suzuki, Nobuyasu; Izawa, Hiroyuki; Sagi, Kazuyuki; Chiba, Akira; Nakanishi, Eiji; Murata, Masahiro; Tsuji, Takashi
PATENT ASSIGNEE(S): Ajinomoto Co., Inc., Japan
SOURCE: PCT Int. Appl., 137 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002016329	A1	20020228	WO 2001-JP7039	20010815

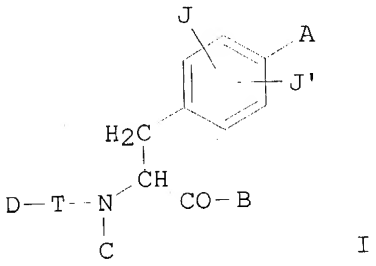
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2001078740	A5	20020304	AU 2001-78740		20010815
EP 1288205	A1	20030305	EP 2001-956901		20010815
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
JP 3440469	B2	20030825	JP 2002-521430		20010815
BR 2001013331	A	20040225	BR 2001-13331		20010815
US 2003220268	A1	20031127	US 2002-300856		20021121
BG 107555	A	20030930	BG 2003-107555		20030214
NO 2003000744	A	20030407	NO 2003-744		20030217
PRIORITY APPLN. INFO.:			JP 2000-248728	A	20000818
			JP 2001-147451	A	20010517
			WO 2001-JP7039	W	20010815

OTHER SOURCE(S): MARPAT 136:217047

GI



I

AB Phenylalanine derivs. [I; A = Q, Q1, Q2, Q3; wherein Arm = cyclic alkyl or aromatic ring containing 1-4 heteroatom(s) selected from O, S, and N; U, V, X = CO, SO2, CR5R6, C(:CR5R6), C:S, S:O, P(O)OH, P(O)H; W = CR7, N; wherein R1 - R7 = H, H, halo, OH, (un)substituted lower alkyl, alkenyl, or alkynyl, cycloalkyl optionally containing a heteroatom in the ring, aryl, heteroaryl, etc.; B = HO, lower alkoxy, hydroxyamino; C = H, lower alkyl, alkenyl, alkynyl, cycloalkyl-lower alkyl (optionally containing an heteroatom in the ring), aryl-lower alkyl, heteroaryl-lower alkyl; D = lower alkyl, alkenyl, alkynyl, cycloalkyl or cycloalkyl-lower alkyl (optionally containing an heteroatom in the ring), aryl, aryl-lower alkyl, heteroaryl-lower alkyl, lower alkoxy, cycloalkyl-lower alkoxy (optionally containing a heteroatom in the ring), aryloxy, heteroaryloxy, etc.; or C and D are linked to each other to form a ring optionally containing 1 or 2 O, N, or S atom(s); T = CO, C:S, SO, SO2, NHCO, NHCS; J, J' = H, halo, lower alkyl, lower alkoxy, NO2] are prepared by the solid phase method using Wang resin. These compds. are useful for the treatment or prevention of inflammatory disease states related to the α4 integrin-dependent adhesion process, e.g. rheumatoid arthritis, inflammatory bowel disease, systemic lupus erythematosus, multiple sclerosis, Sjoegren's syndrome, asthma, psoriasis, allergy, diabetes, cardiovascular diseases, atherosclerosis, restenosis, tumor proliferation, tumor metastasis, and transplant rejection. Thus, a solution of Fmoc-Phe(4-NO2)-OH, 2,6-dichlorobenzoyl chloride, and pyridine in N-methylpyrrolidone was added to Wang resin and stirred at room temperature for 16 h to give Fmoc-Phe(4-NO2)-Wang resin which was deprotected by 20% piperidine in DMF at room temperature for 15 min to afford H-Phe(4-NO2)-Wang resin and then acylated by 2,6-dichlorobenzoyl chloride and 2,6-lutidine in N-methylpyrrolidone at room temperature for 16 h to give 2,6-dichlorobenzoyl-Phe(4-NO2)-Wang resin. The latter compound-bound resin was reduced by

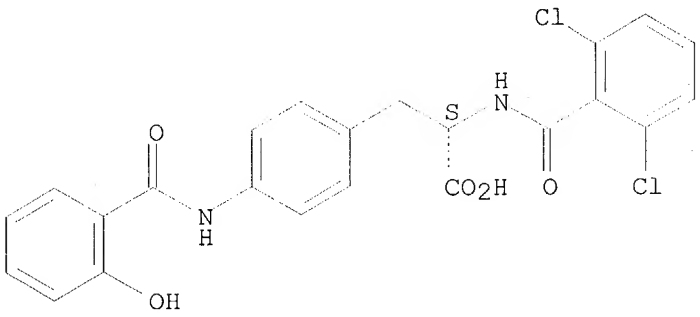
SnCl2.2H2O in EtOH/N-methylpyrrolidone at room temperature for 16 h to 2,6-dichlorobenzoyl-Phe(4-NH2)-Wang resin which was cyclocondensed with Me 2-isocyanatobenzoate in N-methylpyrrolidone at room temperature for 16 h to give 2,6-dichlorobenzoyl-Phe(4-Q)-Wang resin (Q = 1,2,3,4-tetrahydro quinazolin-3-yl) and then methylated by Me iodide in the presence of 18-crown-6 ether and K2CO3 in N-methylpyrrolidone at room temperature for 3 days to give 2,6-dichlorobenzoyl-Phe(4-Q)-Wang resin (Q = 1-methyl-1,2,3,4-tetrahydroquinazolin-3-yl). Resin-cleavage reaction with 5% aqueous CF3CO2H at room temperature for 1 h gave 2,6-dichlorobenzoyl-Phe(4-Q)-OH (Q = 1-methyl-1,2,3,4-tetrahydroquinazolin-3-yl) (II). II and 2-chloro-6-methylbenzoyl-Phe(4-Q)-OH (Q = 1-methyl-1,2,3,4-tetrahydroquinazolin-3-yl) inhibited the binding of human recombinant VCAM-1 to human T cell Jurikat (ATCC TIB-152) cell expressing integrin α4β1 with IC50 of 1.0 and 0.2 nM, resp.

IT **401906-04-5DP**, Wang resin-bound
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(rejection of)

RN 401906-04-5 HCAPLUS

CN L-Phenylalanine, N-(2,6-dichlorobenzoyl)-4-[(2-hydroxybenzoyl)amino]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 5 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2001:549162 HCAPLUS

DOCUMENT NUMBER: 136:107380

TITLE: Oral delivery of biologically active parathyroid hormone

AUTHOR(S): Leone-Bay, Andrea; Sato, Masahiko; Paton, Duncan; Hunt, Ann H.; Sarubbi, Donald; Carozza, Monica; Chou, James; McDonough, James; Baughman, Robert A.

CORPORATE SOURCE: Emisphere Technologies, Inc., Tarrytown, NY, 10591, USA

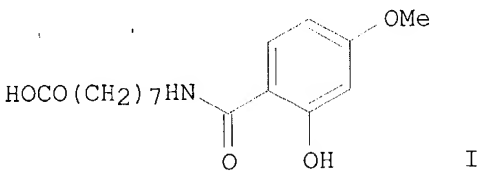
SOURCE: Pharmaceutical Research (2001), 18(7), 964-970
CODEN: PHREEB; ISSN: 0724-8741

PUBLISHER: Kluwer Academic/Plenum Publishers

DOCUMENT TYPE: Journal

LANGUAGE: English

GI

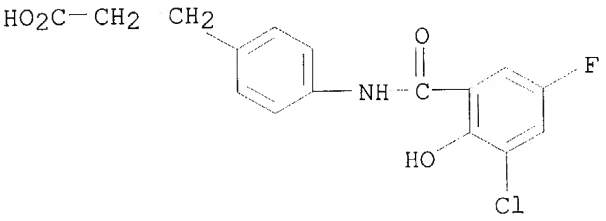


I

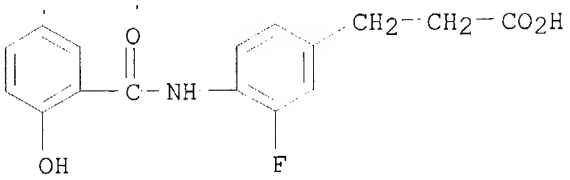
AB Parathyroid hormone (PTH), the only drug known to stimulate bone formation, is a peptide therapeutic indicated in the treatment of osteoporosis. Unfortunately, PTH is only effective when dosed by injection because it has no oral bioavailability. Herein we report the oral absorption of PTH in rats and monkeys facilitated by the novel delivery agent, N-[8-(2-hydroxy-4-methoxy)bensoyl]aminocaprylic acid (I). I was selected from a group of 100 delivery agents based on in vitro chromatog. studies and in vivo screening studies in rats. The PTH/I combination was then tested in monkeys. The interaction of I and PTH was evaluated by NMR spectroscopy. Monkeys were administered an aqueous solution containing I and PTH and mean peak serum PTH concns. of about 3000 pg/mL were obtained. The relative bioavailability of oral PTH was 2.1% relative to s.c. administration. The biol. activity of the orally-delivered PTH was further evaluated in a rat model of osteoporosis. These studies showed that the bone formed following oral PTH/I administration was comparable to that formed following PTH injections. The I mediated absorption of PTH is hypothesized to be the result of a noncovalent interaction between I and PTH. The preliminary evaluation of this interaction by NMR is described. I facilitates the absorption of PTH following oral administration to both rats and monkeys. The orally-absorbed PTH is biol. active as demonstrated in a rat model of osteoporosis.

IT **257951-32-9 345270-28-2 345270-31-7 345270-32-8 345270-34-0 389078-59-5 389078-60-8**
RL: PKT (Pharmacokinetics); BIOL (Biological study)
(oral delivery of biol. active parathyroid hormone)

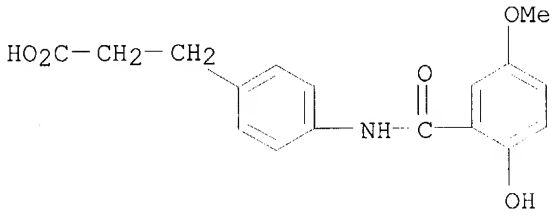
RN 257951-32-9 HCAPLUS
CN Benzenepropanoic acid, 4-[(3-chloro-5-fluoro-2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)



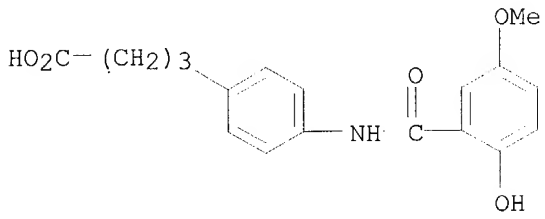
RN 345270-28-2 HCAPLUS
CN Benzenepropanoic acid, 3-fluoro-4-[(2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)



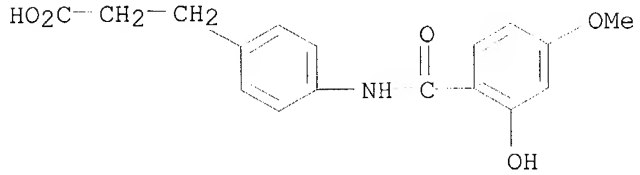
RN 345270-31-7 HCAPLUS
CN Benzenepropanoic acid, 4-[(2-hydroxy-5-methoxybenzoyl)amino]- (9CI) (CA INDEX NAME)



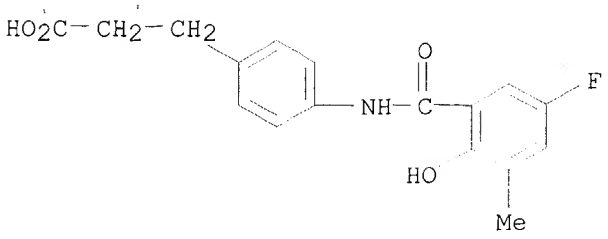
RN 345270-32-8 HCAPLUS
CN Benzenebutanoic acid, 4-[(2-hydroxy-5-methoxybenzoyl)amino]- (9CI) (CA INDEX NAME)



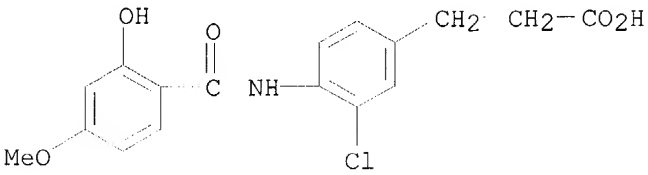
RN 345270-34-0 HCAPLUS
CN Benzenepropanoic acid, 4-[(2-hydroxy-4-methoxybenzoyl)amino]- (9CI) (CA INDEX NAME)



RN 389078-59-5 HCAPLUS
CN Benzenepropanoic acid, 4-[(5-fluoro-2-hydroxy-3-methylbenzoyl)amino]- (9CI) (CA INDEX NAME)



RN 389078-60-8 HCAPLUS
CN Benzenepropanoic acid, 3-chloro-4-[(2-hydroxy-4-methoxybenzoyl)amino]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 6 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:453027 HCAPLUS
DOCUMENT NUMBER: 135:45996
TITLE: Preparation of ω-benzoylaminoalkanoic acids as drug delivery agents
INVENTOR(S): Gschneidner, David; Leone-Bay, Andrea; Wang, Eric; Freeman, John J., Jr.; O'Toole, Doris; Shields, Lynn E.
PATENT ASSIGNEE(S): Emisphere Technologies, Inc., USA
SOURCE: PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

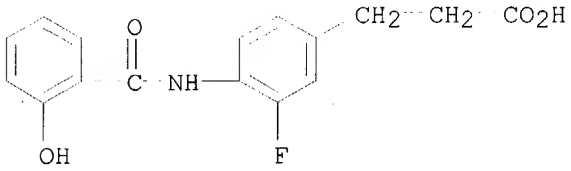
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001044199	A1	20010621	WO 2000-US34329	20001218
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1237872	A1	20020911	EP 2000-986516	20001218
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003516971	T2	20030520	JP 2001-544689	20001218
US 2003216589	A1	20031120	US 2002-168275	20020715

US 6693208 B2 20040217
PRIORITY APPLN. INFO.: US 1999-171213P P 19991216
WO 2000-US34329 W 20001218

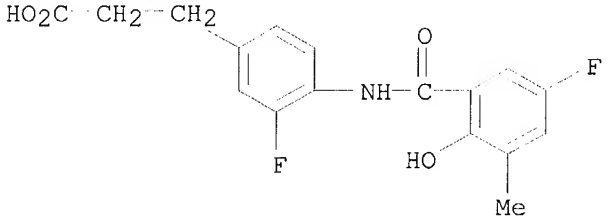
AB Title compds. were prepared Thus, 2,5-(HO)(MeO)C6H3CO2H was O-protected and the chlorinated product amidated by 8-aminocaprylic acid to give, after deprotection, 2,5-(HO)(MeO)C6H3CONH(CH2)7CO2H. Data for biol. activity of title compds. were given.

IT **345270-28-2P 345270-29-3P 345270-31-7P 345270-32-8P 345270-34-0P 345270-37-3P 345270-38-4P**
RL: MOA (Modifier or additive use); SPN (Synthetic preparation); PREP (Preparation); USES (Uses)
(preparation of ω-benzoylaminoalkanoic acids as drug delivery agents)

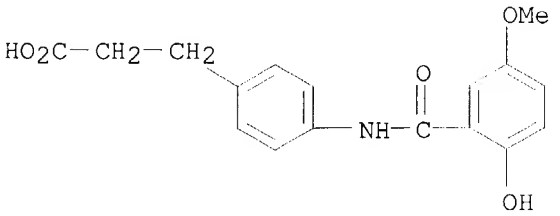
RN 345270-28-2 HCAPLUS
CN Benzenepropanoic acid, 3-fluoro-4-[(2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)



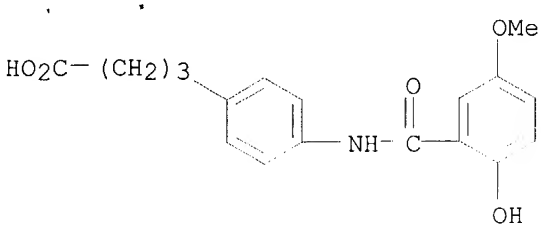
RN 345270-29-3 HCAPLUS
CN Benzenepropanoic acid, 3-fluoro-4-[(5-fluoro-2-hydroxy-3-methylbenzoyl)amino]- (9CI) (CA INDEX NAME)



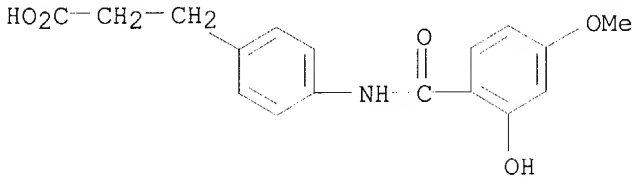
RN 345270-31-7 HCAPLUS
CN Benzenepropanoic acid, 4-[(2-hydroxy-5-methoxybenzoyl)amino]- (9CI) (CA INDEX NAME)



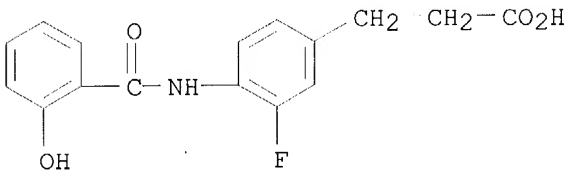
RN 345270-32-8 HCAPLUS
CN Benzenebutanoic acid, 4-[(2-hydroxy-5-methoxybenzoyl)amino]- (9CI) (CA INDEX NAME)



RN 345270-34-0 HCAPLUS
CN Benzenepropanoic acid, 4-[(2-hydroxy-4-methoxybenzoyl)amino]- (9CI) (CA INDEX NAME)

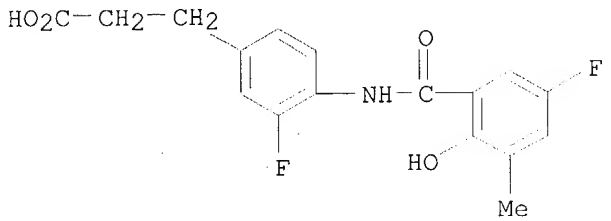


RN 345270-37-3 HCAPLUS
CN Benzenepropanoic acid, 3-fluoro-4-[(2-hydroxybenzoyl)amino]-, monosodium salt (9CI) (CA INDEX NAME)



● Na

RN 345270-38-4 HCAPLUS
CN Benzenepropanoic acid, 3-fluoro-4-[(5-fluoro-2-hydroxy-3-methylbenzoyl)amino]-, monosodium salt (9CI) (CA INDEX NAME)



● Na

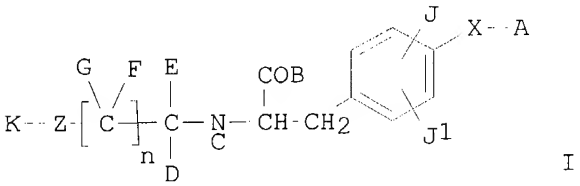
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 7 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:380546 HCAPLUS
DOCUMENT NUMBER: 134:367194
TITLE: Preparation of novel phenylalanine derivatives as α4-integrin inhibitors
INVENTOR(S): Tanaka, Yasuhiro; Yoshimura, Toshihiko; Izawa, Hiroyuki; Ejima, Chieko; Kojima, Mitsuhiko; Atake, Yuko; Nakanishi, Eiji; Suzuki, Nobuyasu; Makino, Shingo; Suzuki, Manabu; Murata, Masahiro
PATENT ASSIGNEE(S): Ajinomoto Co., Inc., Japan
SOURCE: PCT Int. Appl., 155 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001036376	A1	20010525	WO 2000-JP8152	20001120
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2001014165	A5	20010530	AU 2001-14165	20001120
EP 1233013	A1	20020821	EP 2000-976347	20001120
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2003149083	A1	20030807	US 2002-150067	20020520

PRIORITY APPLN. INFO.: JP 1999-328468 A 19991118
JP 2000-197139 A 20000629
WO 2000-JP8152 W 20001120

OTHER SOURCE(S): MARPAT 134:367194
GI



I

AB Phenylalanine derivs. represented by general formula (I) or pharmaceutically acceptable salts thereof [wherein X represents an interat. bond, O, OSO2, N-(un)substituted NH, NHCO, NHSO2, NHCONH, or NH(CS)NH, CO; Y and Z represent each CO, SO, or SO2; A represents a

specific substituted Ph group or nitrogen-containing heterocycle such as aromatic-fused pyrimidinedione or pyrimidinone, 2,4- or 2,5-imidazolidinedione, or 5-imidazolone; C represents hydrogen, lower alkyl, lower alkenyl, lower alkynyl, cyclic alkyl-lower alkyl optionally containing heteroatoms in the ring, aryl-lower alkyl, heteroaryl-lower alkyl; D and E represent each lower alkyl, lower alkenyl, lower alkynyl, cyclic alkyl-lower alkyl optionally containing heteroatoms in the ring, aryl-lower alkyl, heteroaryl-lower alkyl, etc. or D and E may be bonded to each other to form a ring optionally containing 1 or 2 O, N, or S in the ring; F and G represent each hydrogen, lower alkyl, lower alkenyl, lower alkynyl, cyclic alkyl-lower alkyl optionally containing heteroatoms in the ring, aryl-lower alkyl, heteroaryl-lower alkyl, etc. or F and G may be bonded to each other to form a ring; n is from 0 to 2; K represents OR7, NR7R8, NHNR7R8, SR7, or R7; R7 and R8 represents H, lower alkyl, etc.; and J and J' represent each hydrogen, halogeno, lower alkyl, lower alkoxy, or NO2] are prepared These derivs. and analogs thereof show an α4 integrin inhibitory activity and are usable as remedies for various diseases relating to α4 integrin, such as inflammatory diseases related to α4 integrin-dependent adhesion process, arthritis, inflammatory intestinal diseases, systemic lupus erythematosus, multiple sclerosis, Sjoegren syndrome, psoriasis, allergy, diabetes, cardiovascular diseases, arteriosclerosis, restenosis, tumor proliferation, tumor metastasis, or transplant rejection. Thus, O-(2,6-dichlorobenzyl)-L-tyrosine bound to Wang resin was allowed to react with diethylmalonic acid, HOAt, 2-dimethylaminoisopropyl chloride hydrochloride (DIC), and N-methyl-2-pyrrolidinone (NMP) at room temperature for 16 h, washed with DMF five times, and condensed with pyrroline using HOAt, DIC, and NMP, followed by oxidation with OsO4 in dioxane at room temperature for 16 and resin-cleavage in aqueous CF3CO2H to give N-[2-[(cis-2,4-dihydroxypyrrolidin-1-yl)carbonyl]-2-ethylbutanoyl]-O-(2,6-dichlorobenzyl)-L-tyrosine (II). II and N-[2-[(pyrrolidin-1-yl)carbonyl]-2-ethylbutanoyl]-4-(2,6-dichlorobenzoylamino)-L-phenylalanine inhibited the binding of human recombinant VCAM-1 to human B lymphoma cell line expressing integrinα4β7 with IC50 of ≤0.02 μmol/L.

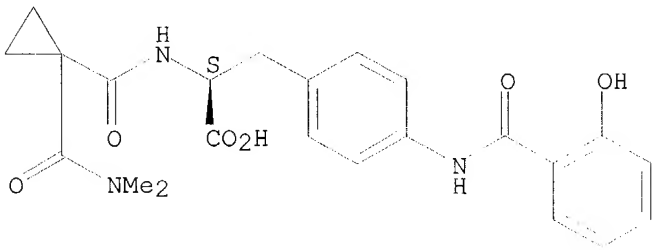
IT **340717-24-0P 340717-60-4P 340717-61-5P 340717-62-6P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of novel phenylalanine derivs. as α4-integrin inhibitors)

RN 340717-24-0 HCAPLUS

CN L-Phenylalanine, N-[[1-[(dimethylamino)carbonyl]cyclopropyl]carbonyl]-4-[(2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)

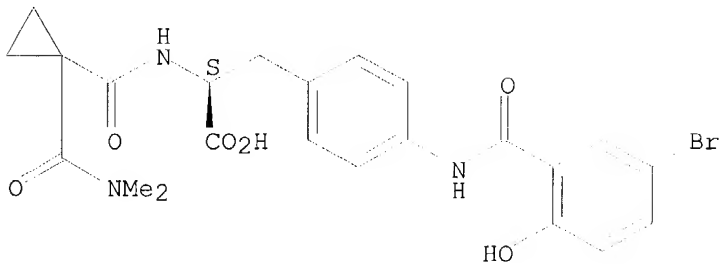
Absolute stereochemistry.



RN 340717-60-4 HCAPLUS

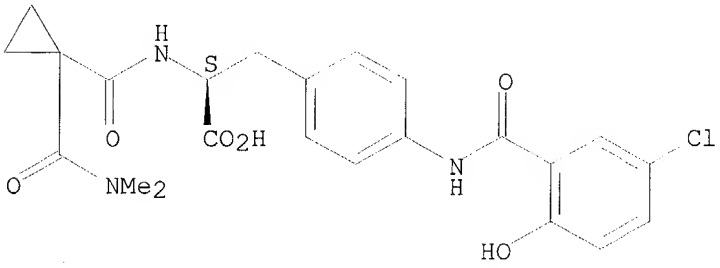
CN L-Phenylalanine, 4-[(5-bromo-2-hydroxybenzoyl)amino]-N-[[1-[(dimethylamino)carbonyl]cyclopropyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



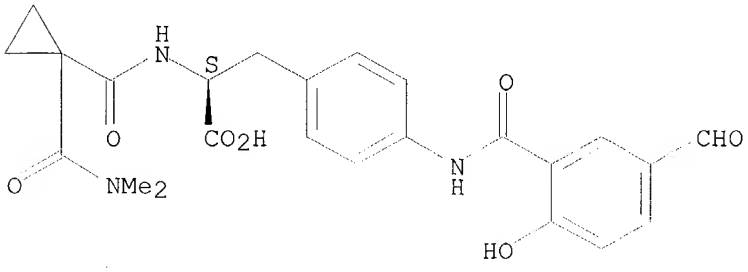
RN 340717-61-5 HCAPLUS
CN L-Phenylalanine, 4-[(5-chloro-2-hydroxybenzoyl)amino]-N-[[1-[(dimethylamino)carbonyl]cyclopropyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 340717-62-6 HCAPLUS
CN L-Phenylalanine, N-[[1-[(dimethylamino)carbonyl]cyclopropyl]carbonyl]-4-[(5-formyl-2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 8 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:297631 HCAPLUS
DOCUMENT NUMBER: 134:316090
TITLE: Active agent transport systems
INVENTOR(S): Milstein, Sam J.; Leone-Bay, Andrea; Sarubbi, Donald J.; Leipold, Harry

PATENT ASSIGNEE(S): Emisphere Technologies, Inc., USA
SOURCE: U.S., 73 pp., Cont.-in-part of U.S. 6,099,856.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 30
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6221367	B1	20010424	US 1997-939939	19970929
US 5443841	A	19950822	US 1992-920346	19920727
US 5451410	A	19950919	US 1993-51019	19930422
US 5578323	A	19961126	US 1993-76803	19930614
US 5447728	A	19950905	US 1993-168776	19931216
US 5792451	A	19980811	US 1994-205511	19940302
US 5541155	A	19960730	US 1994-231623	19940422
US 5629020	A	19970513	US 1994-231622	19940422
US 5693338	A	19971202	US 1994-315200	19940929
US 6331318	B1	20011218	US 1994-316404	19940930
ZA 9408342	A	19950622	ZA 1994-8342	19941024
US 5714167	A	19980203	US 1994-328932	19941025
US 6099856	A	20000808	US 1996-763183	19961210
US 6344213	B1	20020205	US 1997-820694	19970318
CA 2304951	AA	19990408	CA 1998-2304951	19980929
WO 9916427	A1	19990408	WO 1998-US20548	19980929
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9895136	A1	19990423	AU 1998-95136	19980929
AU 735693	B2	20010712		
EP 1021169	A1	20000726	EP 1998-948597	19980929
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001517694	T2	20011009	JP 2000-513565	19980929
AU 771024	B2	20040311	AU 2000-72261	20001214
AU 771434	B2	20040325	AU 2000-72260	20001214
US 2001039258	A1	20011108	US 2001-760307	20010111
US 2002127202	A1	20020912	US 2001-5511	20011107
US 2002155993	A1	20021024	US 2002-125836	20020419
US 6663898	B2	20031216		
US 2003198658	A1	20031023	US 2003-443713	20030521

PRIORITY APPLN. INFO.:

US 1992-898909	B2	19920615
US 1992-920346	A2	19920727
US 1993-51019	B2	19930422
US 1993-76803	A2	19930614
US 1993-143571	B2	19931026
US 1993-168776	A2	19931216
US 1994-205511	A2	19940302
US 1994-205511	A2	19940302
US 1994-231622	A2	19940422
US 1994-231623	B2	19940422
WO 1994-US4560	A2	19940422
US 1994-315200	A2	19940929
US 1994-316404	A2	19940930

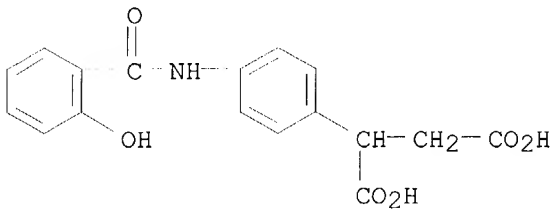
US	1994-328932	A2 19941025
US	1996-17902P	P 19960329
US	1996-763183	A2 19961210
US	1997-820694	A2 19970318
US	1997-939939	A 19970929
AU	1998-62756	A3 19980206
WO	1998-US20548	W 19980929
US	2001-929530	A1 20010813
US	2002-125836	A1 20020419

AB Methods for transporting a biol. active agent across a cellular membrane or a lipid bilayer includes the steps of: (a) providing a biol. active agent which can exist in a native conformational state, a denatured conformational state, and an intermediate conformational state which is reversible to the native state and which is conformationally between the native and denatured states; (b) exposing the biol. active agent to a complexing perturbant to reversibly transform the biol. active agent to the intermediate state and to form a transportable supramol. complex; and (c) exposing the membrane or bilayer to the supramol. complex, to transport the biol. active agent across the membrane or bilayer. The perturbant has a mol. weight between about 150 and about 600 daltons, and contains at least one hydrophilic moiety and at least one hydrophobic moiety. The supramol. complex comprises the perturbant non-covalently bound or complexed with the biol. active agent. In the present invention, the biol. active agent does not form a microsphere after interacting with the perturbant. A method for preparing an orally administrable biol. active agent comprising steps (a) and (b) above is also provided as are oral delivery compns. Addnl., mimetics and methods for preparing mimetics are contemplated. One example gives penetrant phenylsulfonyl-p-aminobenzoic acid effect on α-interferon.

IT **183990-74-1**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(active agent transport systems containing complexing pertubants and biol. agents)

RN 183990-74-1 HCAPLUS

CN Butanedioic acid, [4-[(2-hydroxybenzoyl)amino]phenyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 721 THERE ARE 721 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 9 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:492070 HCAPLUS
DOCUMENT NUMBER: 133:109955
TITLE: Amino acid derivatives and compositions therewith for delivering active agents
INVENTOR(S): Leone-Bay, Andrea; Ho, Koc-kan; Sarubbi, Donald J.; Leipold, Harry R.
PATENT ASSIGNEE(S): Emisphere Technologies, Inc., USA

SOURCE: U.S., 44 pp., Cont.-in-part of PCT 9736480.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 30
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6090958	A	20000718	US 1997-797816	19970207
WO 9736480	A1	19971009	WO 1997-US5128	19970318
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2319672	AA	19980813	CA 1998-2319672	19980206
CA 2319680	AA	19980813	CA 1998-2319680	19980206
WO 9834632	A1	19980813	WO 1998-US2619	19980206
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, US, US, US, US, US, US, US, US, US, US, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9862756	A1	19980826	AU 1998-62756	19980206
AU 738735	B2	20010927		
EP 993831	A2	20000419	EP 1999-117292	19980206
EP 993831	A3	20010502		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
EP 1015008	A1	20000705	EP 1998-905042	19980206
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
EP 1093819	A2	20010425	EP 2000-122704	19980206
EP 1093819	A3	20030514		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001131090	A2	20010515	JP 2000-311231	19980206
JP 2001139494	A2	20010522	JP 2000-311230	19980206
JP 2001513080	T2	20010828	JP 1998-535034	19980206
NZ 337131	A	20010831	NZ 1998-337131	19980206
MX 9907290	A	20000531	MX 1999-7290	19990806
NZ 507275	A	20011130	NZ 2000-507275	20001003
NZ 507276	A	20020201	NZ 2000-507276	20001003
AU 771024	B2	20040311	AU 2000-72261	20001214
AU 771434	B2	20040325	AU 2000-72260	20001214

PRIORITY APPLN. INFO.:

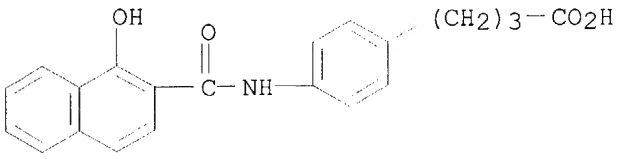
US 1996-17902P	P	19960329
WO 1997-US5128	A2	19970318
US 1996-17902	A1	19960329
US 1997-796334	A	19970207
US 1997-796335	A	19970207
US 1997-796336	A	19970207
US 1997-796337	A	19970207

US 1997-796338	A	19970207
US 1997-796339	A	19970207
US 1997-796340	A	19970207
US 1997-796341	A	19970207
US 1997-797100	A	19970207
US 1997-797813	A	19970207
US 1997-797816	A	19970207
US 1997-797817	A	19970207
US 1997-797820	A	19970207
AU 1998-62756	A3	19980206
CA 1998-2279331	A3	19980206
EP 1998-905042	A3	19980206
EP 1999-117292	A3	19980206
JP 1998-535034	A3	19980206
NZ 1998-337131	A1	19980206
WO 1998-US2619	W	19980206

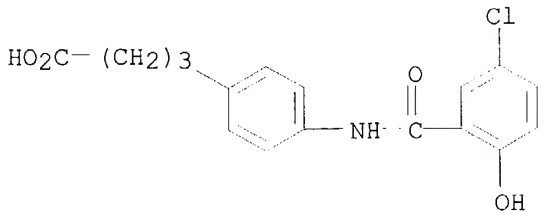
AB Carrier compds., especially amino acid derivs., and compns. therewith which are useful in the delivery of active agents, e.g. peptides, mucopolysaccharides, carbohydrates, and lipids, are provided. Methods of administration and preparation are provided as well. An intracolonic dosing composition containing parathyroid hormone 25 μg/kg, 4-[4-(phenoxyacetyl)aminophenyl]butyric acid as carrier 100 mg/kg in 25% aqueous propylene glycol was prepared

IT **209961-45-5P 209961-80-8P 209961-83-1P**
209961-85-3P 209962-03-8P 209962-04-9P
209962-15-2P 209962-17-4P 211511-75-0P
211511-91-0P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(amino acid derivs. as drug carriers for biol. active components)

RN 209961-45-5 HCAPLUS
CN Benzenebutanoic acid, 4-[[(1-hydroxy-2-naphthalenyl)carbonyl]amino]- (9CI) (CA INDEX NAME)

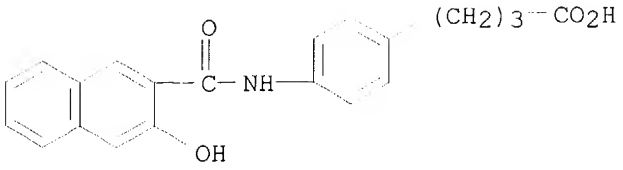


RN 209961-80-8 HCAPLUS
CN Benzenebutanoic acid, 4-[(5-chloro-2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)

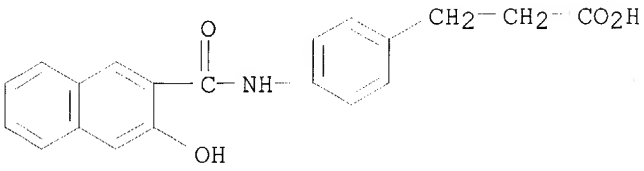


RN 209961-83-1 HCAPLUS
CN Benzenebutanoic acid, 4-[[(3-hydroxy-2-naphthalenyl)carbonyl]amino]- (9CI)

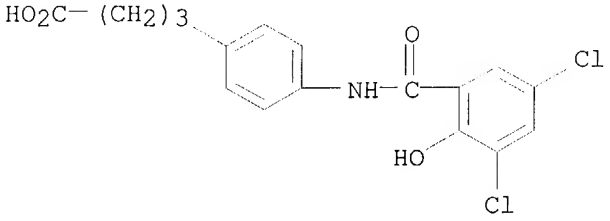
(CA INDEX NAME)



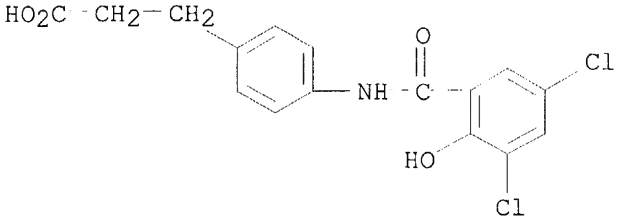
RN 209961-85-3 HCAPLUS
CN Benzenepropanoic acid, 4-[[(3-hydroxy-2-naphthalenyl)carbonyl]amino]- (9CI) (CA INDEX NAME)



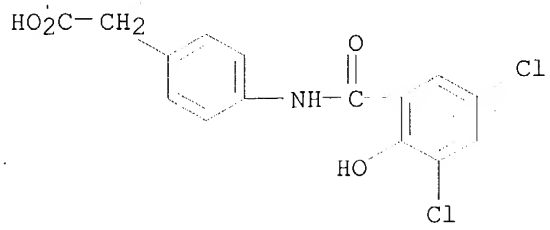
RN 209962-03-8 HCAPLUS
CN Benzenebutanoic acid, 4-[(3,5-dichloro-2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)



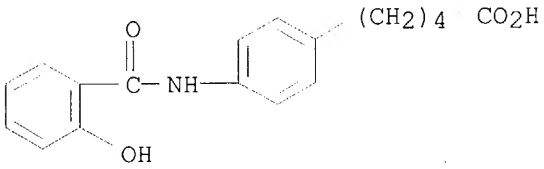
RN 209962-04-9 HCAPLUS
CN Benzenepropanoic acid, 4-[(3,5-dichloro-2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)



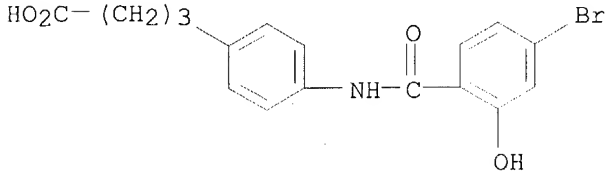
RN 209962-15-2 HCAPLUS
CN Benzeneacetic acid, 4-[(3,5-dichloro-2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)



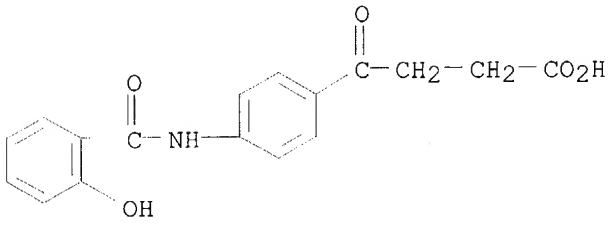
RN 209962-17-4 HCAPLUS
CN Benzenepentanoic acid, 4-[(2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)



RN 211511-75-0 HCAPLUS
CN Benzenebutanoic acid, 4-[(4-bromo-2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)



RN 211511-91-0 HCAPLUS
CN Benzenebutanoic acid, 4-[(2-hydroxybenzoyl)amino]-γ-oxo- (9CI) (CA INDEX NAME)



L17 ANSWER 10 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:475505 HCAPLUS
DOCUMENT NUMBER: 133:109945
TITLE: Polymeric delivery agents comprising a polymer conjugated to a modified amino acid or derivative thereof
INVENTOR(S): Milstein, Sam J.; Barantsevitch, Eugene N.; Wang, Nai Fang; Liao, Jun; Smart, John E.; Conticello, Richard

D.; Ottenbrite, Raphael M.
PATENT ASSIGNEE(S): Emisphere Technologies, Inc., USA; Virginia Commonwealth University
SOURCE: PCT Int. Appl., 91 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

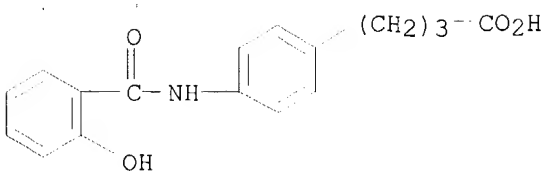
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000040203	A2	20000713	WO 2000-US476	20000107
WO 2000040203	A3	20001214		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2358463	AA	20000713	CA 2000-2358463	20000107
EP 1146860	A2	20011024	EP 2000-914419	20000107
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 2000008590	A	20011030	BR 2000-8590	20000107
JP 2002534363	T2	20021015	JP 2000-591961	20000107
NZ 512581	A	20021220	NZ 2000-512581	20000107
ZA 2001005213	A	20020717	ZA 2001-5213	20010625
US 6627228	B1	20030930	US 2001-889005	20011009
US 2003232085	A1	20031218	US 2003-447608	20030528

PRIORITY APPLN. INFO.:
US 1999-115273P P 19990108
WO 2000-US476 W 20000107
US 2001-889005 A1 20011009

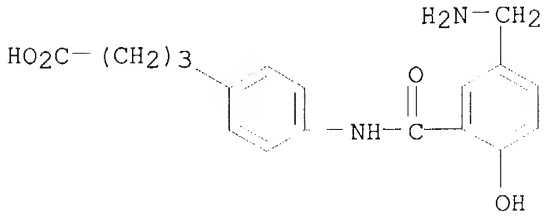
AB Polymeric delivery agents comprising a polymer conjugated to a modified amino acid or derivative thereof, delivery agent compds. and compns. comprising them which are useful in the delivery of active agents are provided. Poly(N-acryloxysuccinimide) was conjugated with N-(5-aminomethylsalicyloyl)-8-aminocaprylic acid (preparation given). Oral and intracolonic delivery composition comprising human growth hormone and above conjugate was administered to rats. At a dose of 200 mg/kg conjugate, the actual amount of delivery agent dosed was 20 mg/kg. With such a concentration of delivery agent complexed with polymer there was evidence of systemic delivery.

IT **177653-18-8P 283599-46-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(polymeric delivery agents comprising polymer conjugated to modified amino acid or derivative thereof)

RN 177653-18-8 HCAPLUS
CN Benzenebutanoic acid, 4-[(2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)



RN 283599-46-2 HCAPLUS
CN Benzenebutanoic acid, 4-[[5-(aminomethyl)-2-hydroxybenzoyl]amino]- (9CI) (CA INDEX NAME)



L17 ANSWER 11 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:117018 HCAPLUS
DOCUMENT NUMBER: 132:151567
TITLE: Preparation of arylamidoalkylcarboxylic acids and compositions for delivering active agents.
INVENTOR(S): Gschneidner, David; Leone-Bay, Andrea; Wang, Eric; Errigo, Lynn; Kraft, Kelly; Moye-Sherman, Destardi; Ho, Koc-Kan; Press, Jeffrey Bruce; Wang, Nai Fang
PATENT ASSIGNEE(S): Emisphere Technologies, Inc., USA
SOURCE: PCT Int. Appl., 53 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000007979	A2	20000217	WO 1999-US17974	19990806
WO 2000007979	A3	20000518		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2339765	AA	20000217	CA 1999-2339765	19990806
AU 9954711	A1	20000228	AU 1999-54711	19990806
EP 1102742	A2	20010530	EP 1999-940967	19990806
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 9912975	A	20010925	BR 1999-12975	19990806

TR 200100366	T2	20011121	TR 2001-20010036619990806	
JP 2002522413	T2	20020723	JP 2000-563614	19990806
NZ 509410	A	20030829	NZ 1999-509410	19990806
ZA 2001000470	A	20010820	ZA 2001-470	20010117

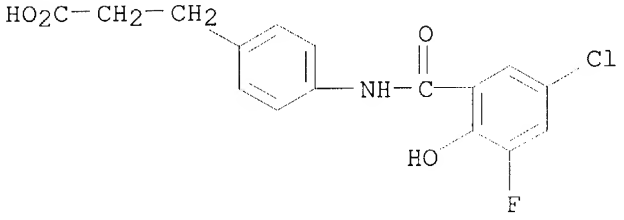
PRIORITY APPLN. INFO.:

US 1998-95778P	P	19980807
US 1998-98500P	P	19980831
US 1998-108366P	P	19981113
US 1999-119207P	P	19990205
WO 1999-US17974	W	19990806

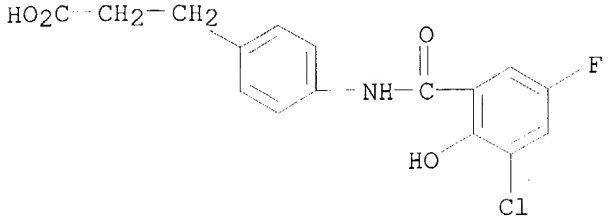
AB 135 Title compds. are claimed. Thus, Me azeloyl chloride was added dropwise to 2-amino-p-cresol in aqueous NaOH at 0° to give a residue which was stirred with aqueous NaOH in THF to give 4-HO-5-MeC6H3NHCO(CH2)7CO2H. Title compds. at 100-300 mg/kg with parathyroid hormone at 25-200 μg orally or intracolonically in rats gave peak serum parathyroid hormone levels of 5-1459.71 pg/mL.

IT **257951-31-8P 257951-32-9P 257951-33-0P**
257951-34-1P 257951-35-2P 257951-38-5P
257951-39-6P 257951-40-9P 257951-41-0P
257951-44-3P 257951-45-4P 257951-97-6P
257951-98-7P 257952-02-6P 257952-19-5P
257952-40-2P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of arylamidoalkylcarboxylic acids and compns. for delivering active agents)

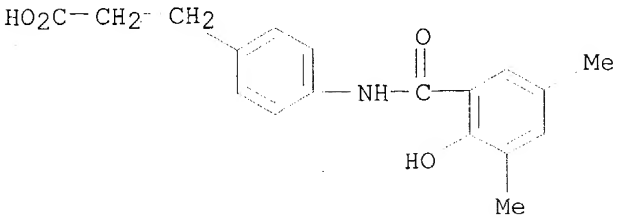
RN 257951-31-8 HCAPLUS
CN Benzenepropanoic acid, 4-[(5-chloro-3-fluoro-2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)



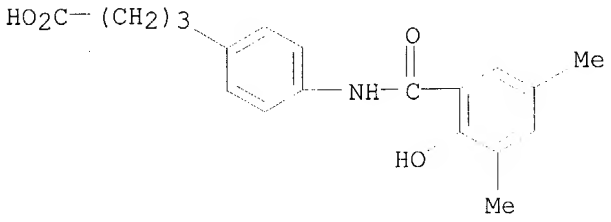
RN 257951-32-9 HCAPLUS
CN Benzenepropanoic acid, 4-[(3-chloro-5-fluoro-2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)



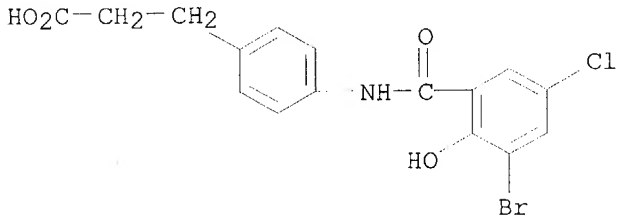
RN 257951-33-0 HCAPLUS
CN Benzenepropanoic acid, 4-[(2-hydroxy-3,5-dimethylbenzoyl)amino]- (9CI) (CA INDEX NAME)



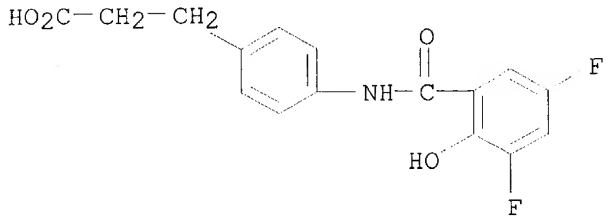
RN 257951-34-1 HCAPLUS
CN Benzenebutanoic acid, 4-[(2-hydroxy-3,5-dimethylbenzoyl)amino]- (9CI) (CA INDEX NAME)



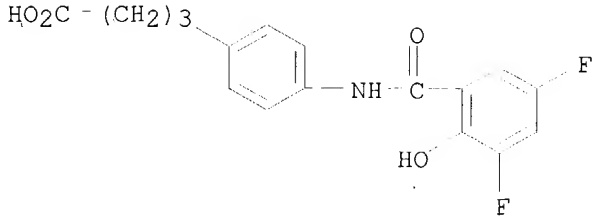
RN 257951-35-2 HCAPLUS
CN Benzenepropanoic acid, 4-[(3-bromo-5-chloro-2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)



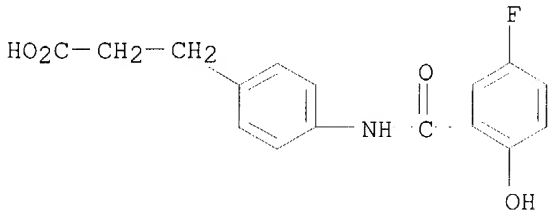
RN 257951-38-5 HCAPLUS
CN Benzenepropanoic acid, 4-[(3,5-difluoro-2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)



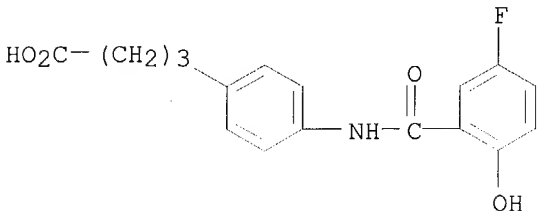
RN 257951-39-6 HCAPLUS
CN Benzenebutanoic acid, 4-[(3,5-difluoro-2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)



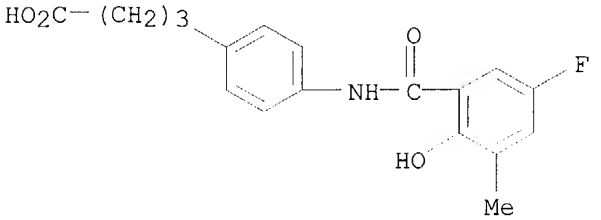
RN 257951-40-9 HCAPLUS
CN Benzenepropanoic acid, 4-[(5-fluoro-2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)



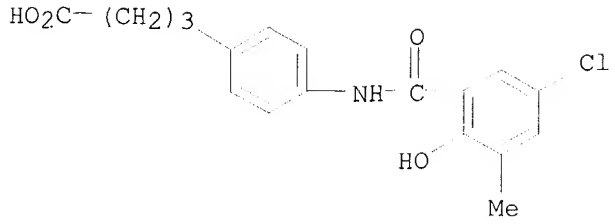
RN 257951-41-0 HCAPLUS
CN Benzenebutanoic acid, 4-[(5-fluoro-2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)



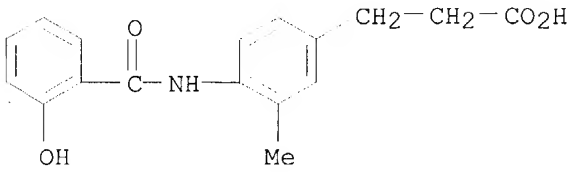
RN 257951-44-3 HCAPLUS
CN Benzenebutanoic acid, 4-[(5-fluoro-2-hydroxy-3-methylbenzoyl)amino]- (9CI) (CA INDEX NAME)



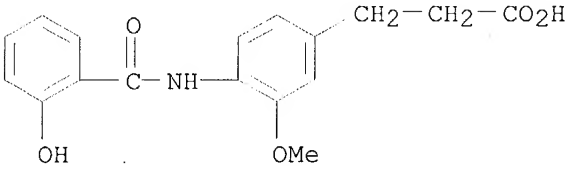
RN 257951-45-4 HCAPLUS
CN Benzenebutanoic acid, 4-[(5-chloro-2-hydroxy-3-methylbenzoyl)amino]- (9CI) (CA INDEX NAME)



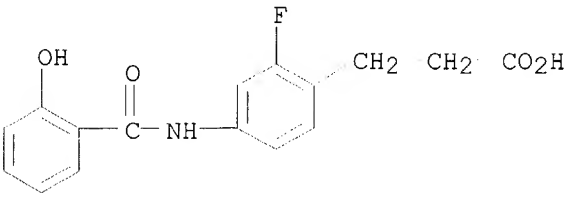
RN 257951-97-6 HCAPLUS
CN Benzenepropanoic acid, 4-[(2-hydroxybenzoyl)amino]-3-methyl- (9CI) (CA INDEX NAME)



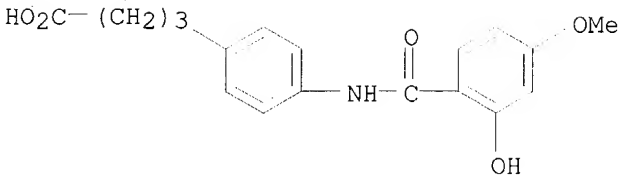
RN 257951-98-7 HCAPLUS
CN Benzenepropanoic acid, 4-[(2-hydroxybenzoyl)amino]-3-methoxy- (9CI) (CA INDEX NAME)



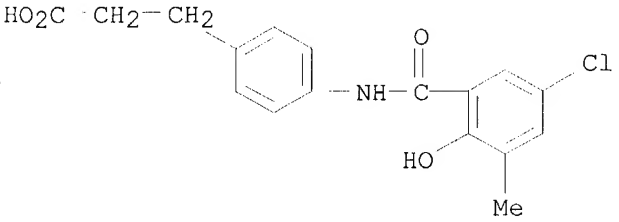
RN 257952-02-6 HCAPLUS
CN Benzenepropanoic acid, 2-fluoro-4-[(2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)



RN 257952-19-5 HCAPLUS
CN Benzenebutanoic acid, 4-[(2-hydroxy-4-methoxybenzoyl)amino]- (9CI) (CA INDEX NAME)



RN 257952-40-2 HCAPLUS
CN Benzenepropanoic acid, 4-[(5-chloro-2-hydroxy-3-methylbenzoyl)amino]-
(9CI) (CA INDEX NAME)



L17 ANSWER 12 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:98355 HCAPLUS
DOCUMENT NUMBER: 132:141984
TITLE: Pulmonary delivery of active agents
INVENTOR(S): Milstein, Sam J.; Smart, John E.; Sarubbi, Donald J.; Carozza, Monica; Flanders, Elizabeth; O'Toole, Doris; Leone-Bay, Andrea; Gschneidner, David
PATENT ASSIGNEE(S): Emisphere Technologies, Inc., USA
SOURCE: PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000006184	A1	20000210	WO 1999-US16957	19990727
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2338358	AA	20000210	CA 1999-2338358	19990727
CA 2338419	AA	20000210	CA 1999-2338419	19990727
WO 2000006534	A1	20000210	WO 1999-US17090	19990727
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU,				

TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 9953210	A1	20000221	AU 1999-53210	19990727
AU 745290	B2	20020321		
AU 9953237	A1	20000221	AU 1999-53237	19990727
AU 751612	B2	20020822		
EP 1100522	A1	20010523	EP 1999-938806	19990727
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
EP 1100771	A1	20010523	EP 1999-938842	19990727
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
TR 200100922	T2	20010921	TR 2001-20010092219990727	
BR 9912694	A	20020102	BR 1999-12694	19990727
JP 2002521455	T2	20020716	JP 2000-562038	19990727
NZ 509239	A	20021025	NZ 1999-509239	19990727
JP 2003517438	T2	20030527	JP 2000-562341	19990727
NZ 509238	A	20030725	NZ 1999-509238	19990727
ZA 2001000227	A	20010807	ZA 2001-227	20010109
ZA 2001000226	A	20010904	ZA 2001-226	20010109
US 6642411	B1	20031104	US 2001-744862	20010419
US 6440929	B1	20020827	US 2001-744777	20010426
US 2003072740	A1	20030417	US 2002-172582	20020614
US 6693073	B2	20040217		
US 2003225300	A1	20031204	US 2003-600413	20030620

PRIORITY APPLN. INFO.:

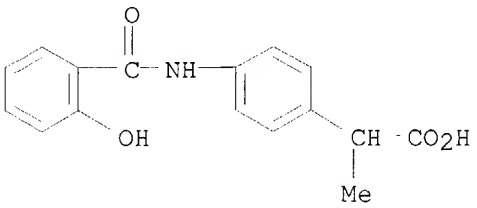
US 1998-94267P	P	19980727
US 1998-104466P	P	19981016
WO 1999-US16957	W	19990727
WO 1999-US17090	W	19990727
US 2001-744862	A1	20010419
US 2001-744777	A1	20010426

OTHER SOURCE(S): MARPAT 132:141984

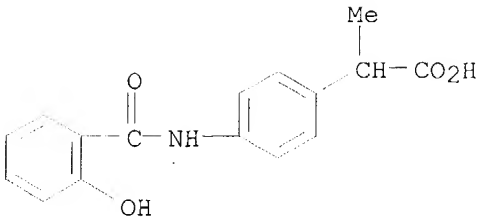
AB Methods of administration of active agents via the pulmonary route are provided. Thus, sodium 2-(4-(N-salicyloyl)aminophenyl)propionate was prepared and 16 mg/kg this compound was mixed with 0.05 mg/kg porcine insulin and administered to rats by lung-spray-IT instillation. The AUC of the formulation wa higher than that without any carrier added.

IT **61126-76-9P 257287-96-0P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(pulmonary delivery of active agents)

RN 61126-76-9 HCAPLUS
CN Benzeneacetic acid, 4-[(2-hydroxybenzoyl)amino]-α-methyl- (9CI) (CA INDEX NAME)



RN 257287-96-0 HCAPLUS
CN Benzeneacetic acid, 4-[(2-hydroxybenzoyl)amino]-α-methyl-, monosodium salt (9CI) (CA INDEX NAME)



● Na

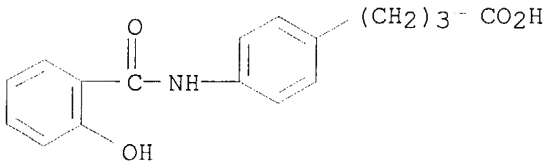
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 13 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:649906 HCAPLUS
DOCUMENT NUMBER: 132:40404
TITLE: Transport of human growth hormone across Caco-2 cells with novel delivery agents: evidence for P-glycoprotein involvement
AUTHOR(S): Wu, S.-J.; Robinson, J. R.
CORPORATE SOURCE: School of Pharmacy, University of Wisconsin, Madison, WI, USA
SOURCE: Journal of Controlled Release (1999), 62(1-2), 171-177
CODEN: JCREEC; ISSN: 0168-3659
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Emisphere Technologies, Inc. has synthesized a series of small mols. which have been shown to improve protein absorption through mucosal tissue. This enhancement is specific between protein and a particular delivery agent. Despite the specificity of interaction, the mechanism of enhanced tissue penetration is still unclear. The purpose of this work is to understand the enhancement mechanism(s) of these delivery agents by using Caco-2 cells as a model membrane. It was found that the bidirectional transepithelial fluxes of human growth hormone (hGH) in the presence of these delivery agents across human intestinal epithelial Caco-2 cell line showed marked asymmetry. Average permeability coefficient values obtained in the apical (AP) to basolateral (BL) direction were lower than those of the reverse (BL to AP) direction. On the other hand, the fluxes for human growth hormone alone were sym. When P-glycoprotein inhibitors were included in the transport medium, the permeability coefficient values of BL to AP direction were significantly decreased while the transport was increased in the reverse direction in the presence of delivery agents. P-glycoprotein inhibitors had no effect on the transport of human growth hormone alone. This study shows that human growth hormone alone can be transported across Caco-2 cells in very limited quantities by passive diffusion, but in the presence of delivery agents, human growth hormone can be effluxed in a P-glycoprotein-mediated fashion. This also indirectly shows that the human growth hormone has become more lipophilic in the presence of delivery agents.

IT **177653-18-8**, e352
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use);

BIOL (Biological study); PROC (Process); USES (Uses)
(transport of human growth hormone across Caco-2 cells with novel delivery agents)
RN 177653-18-8 HCAPLUS
CN Benzenebutanoic acid, 4-[(2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

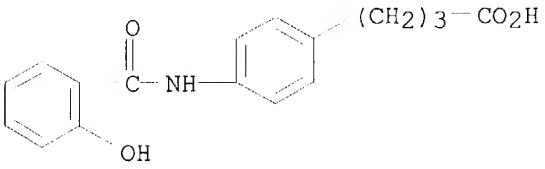
L17 ANSWER 14 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:548469 HCAPLUS
DOCUMENT NUMBER: 131:291168
TITLE: Transcellular and lipophilic complex-enhanced intestinal absorption of human growth hormone
AUTHOR(S): Wu, Sy-Juen; Robinson, Joseph R.
CORPORATE SOURCE: School of Pharmacy, University of Wisconsin-Madison, Madison, WI, 53706, USA
SOURCE: Pharmaceutical Research (1999), 16(8), 1266-1272
CODEN: PHREEB; ISSN: 0724-8741
PUBLISHER: Kluwer Academic/Plenum Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English
AB To evaluate the transcellular mechanism of novel enhancers absorption enhancement of human growth hormone (hGH), by examining the involvement of a P-glycoprotein-like efflux system, changes in membrane fluidity, and membrane damage, Caco-2 cell monolayers were grown on Snapwell filter supports and placed in a side-by-side diffusion apparatus Transport in both the apical to basolateral (AP to BL) and basolateral to apical (BL to AP) direction was measured at different temps. and in the presence of potential inhibitors. Fluorescence anisotropy measurement was used to measure membrane fluidity. The fluorescence anisotropy of DPH- and TMA-DPH-labeled cell suspensions was measured at room temperature LDH (a measure of cytosolic lactate dehydrogenase) leakage assay was used to evaluate cytotoxicity. The bi-directional transepithelial fluxes of hGH in the presence of these novel enhancers across Caco-2 cells showed marked asymmetry. Average permeability coefficient values obtained in the apical to basolateral (AP to BL) direction were lower than those of the reverse (BL to AP) direction. On the other hand, the fluxes for hGH alone were sym. When P-gp-like efflux inhibitors were included in the transport medium, the permeability coefficient value of BL to AP direction was significantly decreased while the transport was increased in the reverse direction in the presence of novel enhancers. In addition, lowering the temperature to 25°C completely eliminated the asymmetry of hGH transport in the presence of novel enhancers. It was also shown by fluorescence anisotropy that these novel enhancers alone only slightly increased membrane fluidity. On the other hand, upon addition of hGH to the novel enhancers, the cell membrane showed a dramatic change as compared to treatment with novel enhancers alone. The results from the LDH assay showed that the novel enhancers and/or hGH did not cause cell damage, at least up to 1 h, and the damage seen at the 2 h point is also much lower than other known enhancers. This study shows that human growth hormone alone cannot be

transported across Caco-2 cells, except in small quantities, by passive diffusion, but in the presence of novel enhancers, human growth hormone permeation is substantial. In addition, the asymmetry of transport of the complexed hGH appears to be due to a P-gp-like efflux system. Assuming that the present substrate specificity of the P-gp-like efflux system shows the same preference for hydrophobic mols. as p-gp, the present work also indirectly shows that human growth hormone has become more lipophilic in the presence of these novel enhancers. Furthermore, membrane fluidity data also supports the premise that these novel enhancers interact and stabilize hGH, to make them more hydrophobic and easier to be transported through cell membranes.

IT **177653-18-8,** E352
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(transcellular and lipophilic complex-enhanced intestinal absorption of human growth hormone)

RN 177653-18-8 HCAPLUS

CN Benzenebutanoic acid, 4-[(2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 15 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1999:211174 HCAPLUS

DOCUMENT NUMBER: 131:23376

TITLE: Barriers and potential solutions to controlled drug delivery across mucosal tissues

AUTHOR(S): Robinson, Joseph R.

CORPORATE SOURCE: School of Pharmacy, University of Wisconsin, Madison, WI, 53706, USA

SOURCE: Polymer Preprints (American Chemical Society, Division of Polymer Chemistry) (1999), 40(1), 254-255
CODEN: ACPPAY; ISSN: 0032-3934

PUBLISHER: American Chemical Society, Division of Polymer Chemistry

DOCUMENT TYPE: Journal

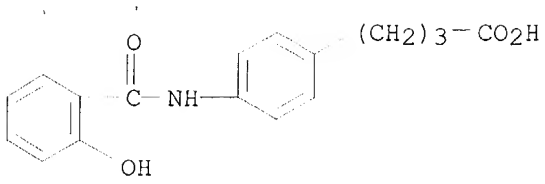
LANGUAGE: English

AB The use of enhancers such as a phenylbutyric acid to improve the transport of human growth hormone across Caco-2 cells and mucosal tissues is discussed.

IT **177653-18-8,** E352
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(barriers to controlled drug delivery across mucosal tissues)

RN 177653-18-8 HCAPLUS

CN Benzenebutanoic acid, 4-[(2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

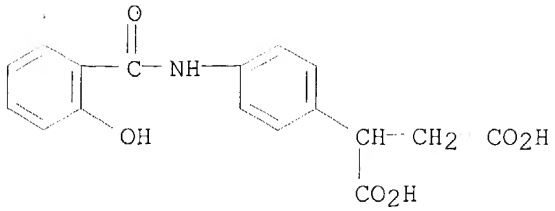
L17 ANSWER 16 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:100747 HCAPLUS
DOCUMENT NUMBER: 130:144204
TITLE: Modified amino acids as carriers for enhanced delivery of active agents
INVENTOR(S): Leone-Bay, Andrea; Ho, Koc-kan; Sarubbi, Donald J.; Milstein, Sam J.
PATENT ASSIGNEE(S): Emisphere Technologies, Inc., USA
SOURCE: U.S., 27 pp., Cont.-in-part of U.S. Ser. No. 414,654. CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 30
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5866536	A	19990202	US 1997-798033	19970206
US 5650386	A	19970722	US 1995-414654	19950331
CN 1190893	A	19980819	CN 1996-192998	19960401
JP 2003313157	A2	20031106	JP 2003-140962	19960401
US 6071510	A	20000606	US 1997-839094	19970423
AU 771024	B2	20040311	AU 2000-72261	20001214
AU 771434	B2	20040325	AU 2000-72260	20001214

PRIORITY APPLN. INFO.:
US 1995-414654 A2 19950331
US 1995-3111P P 19950901
JP 1996-529751 A3 19960401
AU 1998-62756 A3 19980206

AB Carrier compds., compns., and dosage unit forms which are useful in the delivery of active agents are provided. The present invention provides compds. such as 10-salicyloylaminodecanoic acid (I) for delivery of at least one active agent, including peptides, mucopolysaccharides, carbohydrates, or lipids. I prepared from 8-aminocaprylic acid and O-acetylsalicyloyl chloride was mixed with recombinant human growth hormone (rhGH) in a phosphate buffer solution The composition was orally administered to rats at I 200 mg/kg and rhGH 3 mg/kg and delivery was evaluated by an ELISA assay for rhGH; mean peak serum levels of rhGH was .apprx.60.92 ng/mL as compared to <0.1 ng/mL for control group received a composition without I.

IT **183990-74-1**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(modified amino acids as carriers for enhanced delivery of active agents)
RN 183990-74-1 HCAPLUS
CN Butanedioic acid, [4-[(2-hydroxybenzoyl)amino]phenyl]- (9CI) (CA INDEX NAME)



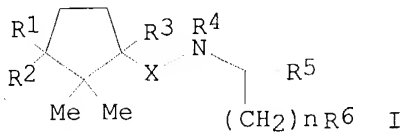
REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 17 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:27805 HCAPLUS
DOCUMENT NUMBER: 130:95843
TITLE: Preparation of cyclopentylcarbonylamino acid as inhibitors of α4β1 mediated cell adhesion
INVENTOR(S): Lobl, Thomas J.; Rishton, Gil; Teegarden, Bradley; Polinsky, Alex; Yamagishi, Masafumi; Tanis, Steven P.; Fisher, Jed F.; Thomas, Edward W.; Chrusciel, Robert A.
PATENT ASSIGNEE(S): Tanabe Seiyaku Co., Ltd., Japan; Pharmacia & Upjohn Company
SOURCE: PCT Int. Appl., 342 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9858902	A1	19981230	WO 1998-US13064	19980623
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9881633	A1	19990104	AU 1998-81633	19980623
EP 991619	A1	20000412	EP 1998-931521	19980623
EP 991619	B1	20030910		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001517246	T2	20011002	JP 1999-504997	19980623
US 6482849	B1	20021119	US 1998-102584	19980623
AT 249421	E	20030915	AT 1998-931521	19980623
ES 2206953	T3	20040516	ES 1998-931521	19980623
US 2003130349	A1	20030710	US 2002-193137	20020712
US 6596752	B1	20030722		

PRIORITY APPLN. INFO.: US 1997-50515P P 19970623
US 1998-102584 A3 19980623
WO 1998-US13064 W 19980623

OTHER SOURCE(S): MARPAT 130:95843
GI



I

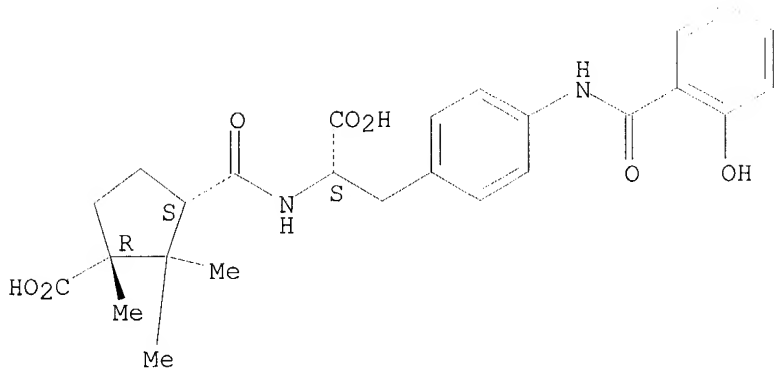
AB Title compds. [I; n = 0, 1; R1 = H, CH3; R2 = CN, CO2H, CONH2, CONHOCH2Ph, NHCOOCH2Ph, etc.; R3 = H, CH3; X = CH, CO; R4 = H, alkyl; R5 = CO2H, CONH2, COOR, etc.; R = alkyl; R6 = aryl, heteroaryl, arylcarbonyl, aarylcarbonylaminoalkyl, etc.], a pharmaceutically acceptable salt, a stereoisomer thereof are prepared as inhibitors of α4β1 mediated adhesion to either VCAM or CS-1 and which can be used for treating or preventing α4β1 adhesion mediated conditions in human such as inflammatory diseases. Thus, (1S-cis)- N-[(3-carboxy-2,2,3-trimethylcyclopentyl)carbonyl]-O-(phenylmethyl)-L-tyrosine was prepared and assayed for inhibition of β1-mediated cell adhesion in vitro.

IT **219495-30-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of cyclopentylcarbonylamino acid as inhibitors of α4β1 mediated cell adhesion)

RN 219495-30-4 HCAPLUS

CN L-Phenylalanine, N-[[(1S,3R)-3-carboxy-2,2,3-trimethylcyclopentyl]carbonyl]-4-[(2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 18 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:745015 HCAPLUS
DOCUMENT NUMBER: 130:3692
TITLE: Preparation of ω-(salicyloylamino)alkanoic acids
INVENTOR(S): Gschneidner, David; O'Toole, Doris; Freeman, John
PATENT ASSIGNEE(S): Emisphere Technologies, Inc., USA
SOURCE: PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9850341	A1	19981112	WO 1998-US8449	19980424
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5962710	A	19991005	US 1997-853752	19970509
AU 9871641	A1	19981127	AU 1998-71641	19980424

PRIORITY APPLN. INFO.: US 1997-853752 19970509
WO 1998-US8449 19980424

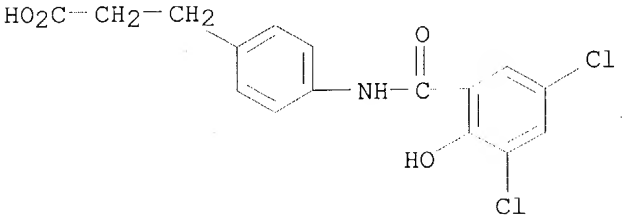
OTHER SOURCE(S): CASREACT 130:3692; MARPAT 130:3692

AB The title method comprises salicyloylation of an ω-aminoalkanoate by HOZ1CO(OZ2CO)nOH [Z1,Z2 = (un)substituted C6H4; n = 1 to .apprx.10].

IT **209962-04-9P**
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of ω-(salicyloylamino)alkanoic acids)

RN 209962-04-9 HCAPLUS

CN Benzenepropanoic acid, 4-[(3,5-dichloro-2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 19 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:548547 HCAPLUS
DOCUMENT NUMBER: 129:180147
TITLE: Compounds and compositions for delivering active agents
INVENTOR(S): Leone-Bay, Andrea; et al.
PATENT ASSIGNEE(S): Emisphere Technologies, Inc., USA
SOURCE: PCT Int. Appl., 147 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 30
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9834632	A1	19980813	WO 1998-US2619	19980206

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, US, US, US, US, US, US, US, US, US, US, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

US 5773647	A	19980630	US 1997-796337	19970207
US 5776888	A	19980707	US 1997-796338	19970207
US 5804688	A	19980908	US 1997-796339	19970207
US 5876710	A	19990302	US 1997-796335	19970207
US 5879681	A	19990309	US 1997-796334	19970207
US 5939381	A	19990817	US 1997-796340	19970207
US 5990166	A	19991123	US 1997-797820	19970207
US 6051561	A	20000418	US 1997-797813	19970207
US 6060513	A	20000509	US 1997-797817	19970207
US 6090958	A	20000718	US 1997-797816	19970207
US 6313088	B1	20011106	US 1997-797100	19970207
US 6358504	B1	20020319	US 1997-796336	19970207
AU 9862756	A1	19980826	AU 1998-62756	19980206
AU 738735	B2	20010927		
EP 1015008	A1	20000705	EP 1998-905042	19980206
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001513080	T2	20010828	JP 1998-535034	19980206
NZ 337131	A	20010831	NZ 1998-337131	19980206
MX 9907290	A	20000531	MX 1999-7290	19990806
AU 771024	B2	20040311	AU 2000-72261	20001214
AU 771434	B2	20040325	AU 2000-72260	20001214
US 2002119910	A1	20020829	US 2000-746548	20001219
US 2003008900	A1	20030109	US 2001-1731	20011031
US 6525020	B2	20030225		
US 2003235612	A1	20031225	US 2003-373582	20030224
US 2004022856	A1	20040205	US 2003-395685	20030324

PRIORITY APPLN. INFO.:

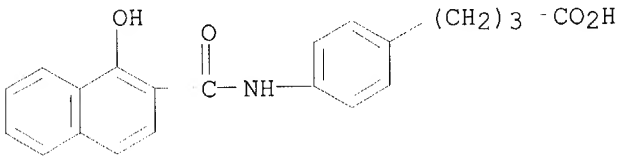
US 1997-796334	A1	19970207
US 1997-796335	A1	19970207
US 1997-796336	A1	19970207
US 1997-796337	A1	19970207
US 1997-796338	A1	19970207
US 1997-796339	A1	19970207
US 1997-796340	A1	19970207
US 1997-796341	A1	19970207
US 1997-797100	A1	19970207
US 1997-797813	A1	19970207
US 1997-797816	A1	19970207
US 1997-797817	A1	19970207
US 1997-797820	A1	19970207
US 1996-17902P	P	19960329
WO 1997-US5128	A2	19970318
AU 1998-62756	A3	19980206
EP 1999-117292	A3	19980206
WO 1998-US2619	W	19980206
US 2000-746548	B1	20001219
US 2001-1731	A1	20011031

AB Carrier compds. and compns. which are useful in the delivery of active agents are provided. The carrier compound can be an amino acid derivative, and the active agent can be a peptide, mucopolysaccharide, carbohydrate, or lipid. Methods of administration, including oral administration, and

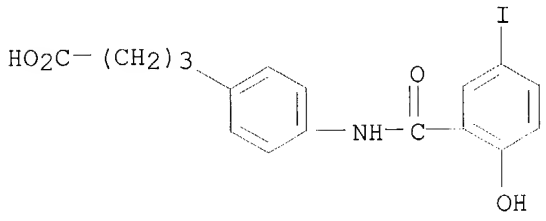
preparation are provided as well. For example, an oral solution contained parathyroid hormone 100 μg, 4-[4-(phenoxyacetyl)aminophenyl]butyric acid (as carrier) 400 mg, and water 1L.

IT **209961-45-5 209961-75-1 209961-80-8 209961-83-1 209961-85-3 209962-03-8 209962-04-9 209962-15-2 209962-17-4 211511-75-0 211511-91-0**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amino acid derivs. as carriers for oral delivery of biol. active agents)

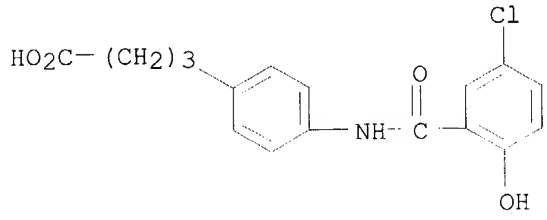
RN 209961-45-5 HCAPLUS
CN Benzenebutanoic acid, 4-[[(1-hydroxy-2-naphthalenyl)carbonyl]amino]- (9CI) (CA INDEX NAME)



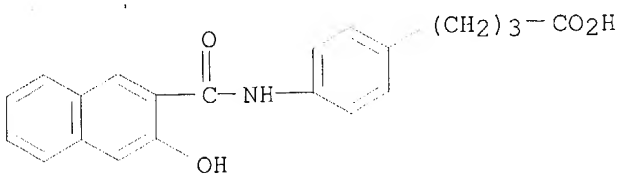
RN 209961-75-1 HCAPLUS
CN Benzenebutanoic acid, 4-[(2-hydroxy-5-iodobenzoyl)amino]- (9CI) (CA INDEX NAME)



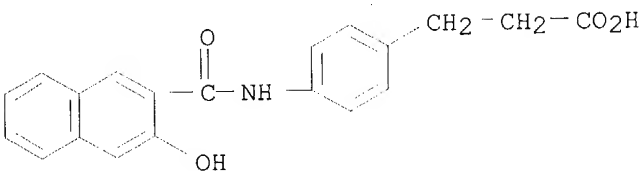
RN 209961-80-8 HCAPLUS
CN Benzenebutanoic acid, 4-[(5-chloro-2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)



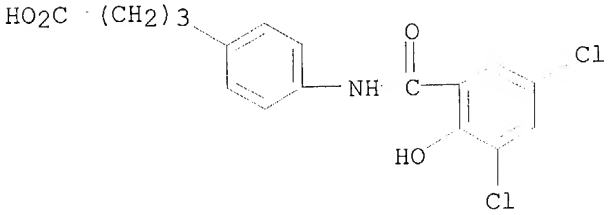
RN 209961-83-1 HCAPLUS
CN Benzenebutanoic acid, 4-[[(3-hydroxy-2-naphthalenyl)carbonyl]amino]- (9CI) (CA INDEX NAME)



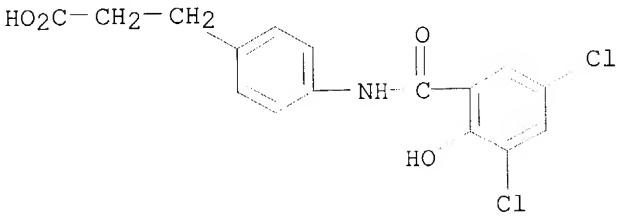
RN 209961-85-3 HCAPLUS
CN Benzenepropanoic acid, 4-[[(3-hydroxy-2-naphthalenyl)carbonyl]amino]- (9CI) (CA INDEX NAME)



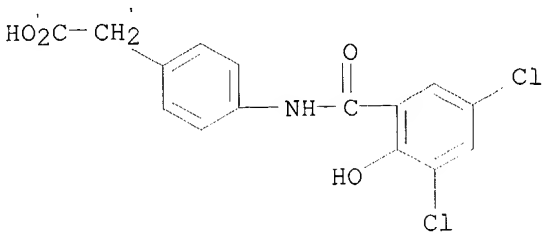
RN 209962-03-8 HCAPLUS
CN Benzenebutanoic acid, 4-[(3,5-dichloro-2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)



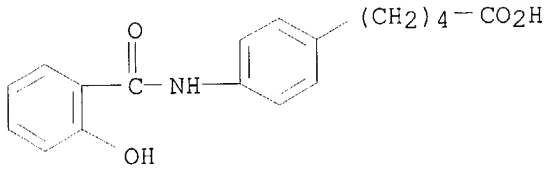
RN 209962-04-9 HCAPLUS
CN Benzenepropanoic acid, 4-[(3,5-dichloro-2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)



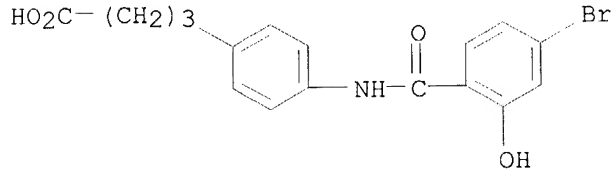
RN 209962-15-2 HCAPLUS
CN Benzeneacetic acid, 4-[(3,5-dichloro-2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)



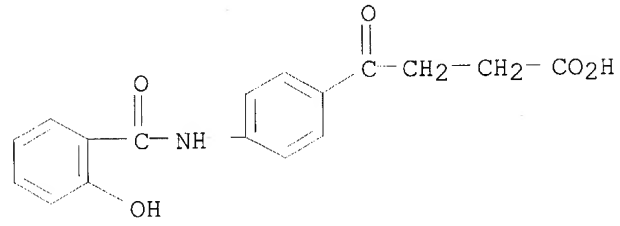
RN 209962-17-4 HCAPLUS
CN Benzenepentanoic acid, 4-[(2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)



RN 211511-75-0 HCAPLUS
CN Benzenebutanoic acid, 4-[(4-bromo-2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)



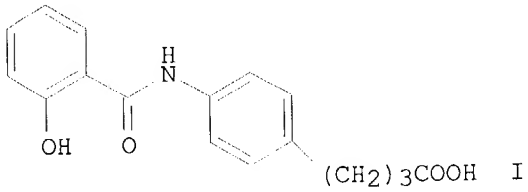
RN 211511-91-0 HCAPLUS
CN Benzenebutanoic acid, 4-[(2-hydroxybenzoyl)amino]-γ-oxo- (9CI) (CA INDEX NAME)



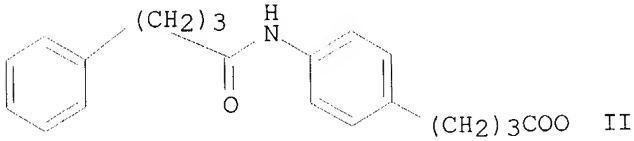
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 20 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:481964 HCAPLUS
DOCUMENT NUMBER: 129:265258
TITLE: Novel delivery agents for induction of oral tolerance
AUTHOR(S): Haas, S.; Meleski, D.; Kutzy, T.; Gerspach, L.; Lercara, C.; O'toole, D.; Devincent, A.; Milstein, S.

CORPORATE SOURCE: Emisphere, Technologies, Inc., Hawthorne, NY, 10532, USA
SOURCE: Proceedings of the International Symposium on Controlled Release of Bioactive Materials (1998), 25th, 621-622
CODEN: PCRMEY; ISSN: 1022-0178
PUBLISHER: Controlled Release Society, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

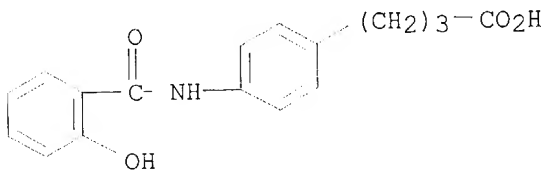


II

AB A single oral dose of 1.0 mg/rat of myelin basic protein (MBP) + EMI-A (I) suppressed the development of clin. disease symptoms of MBP-induced encephalomyelitis to the same extent as five doses of 1.0 mg each of MBP alone, and significantly more than a single dose of MBP alone. Feeding rats 5 doses of 0.1 mg of MBP each in the presence of EMI-B (II) lowered the AUC of the disease course ~60% compared with MBP alone. This suggests that Emisphere's delivery agents may constitute an oral delivery system that can augment the inducing tolerance properties of co-administered proteins, allowing the use of fewer or lower doses than are generally required. This technol. may be useful in the treatment of autoimmune and allergic disorders and for the prevention of allograft rejection.

IT **177653-18-8**, EMI-A
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel delivery agents for induction of oral tolerance)

RN 177653-18-8 HCAPLUS
CN Benzenebutanoic acid, 4-[(2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 21 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:457247 HCAPLUS
DOCUMENT NUMBER: 129:113532
TITLE: Compounds and compositions for delivering active agents
INVENTOR(S): Leone-Bay, Andrea; Wang, Eric; Sarubbi, Donald J.; Leipold, Harry
PATENT ASSIGNEE(S): Emisphere Technologies, Inc., USA
SOURCE: U.S., 34 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 30
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5776888	A	19980707	US 1997-796338	19970207
CA 2319672	AA	19980813	CA 1998-2319672	19980206
CA 2319680	AA	19980813	CA 1998-2319680	19980206
WO 9834632	A1	19980813	WO 1998-US2619	19980206
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, US, US, US, US, US, US, US, US, US, US, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9862756	A1	19980826	AU 1998-62756	19980206
AU 738735	B2	20010927		
EP 993831	A2	20000419	EP 1999-117292	19980206
EP 993831	A3	20010502		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
EP 1015008	A1	20000705	EP 1998-905042	19980206
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
EP 1093819	A2	20010425	EP 2000-122704	19980206
EP 1093819	A3	20030514		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001131090	A2	20010515	JP 2000-311231	19980206
JP 2001139494	A2	20010522	JP 2000-311230	19980206
JP 2001513080	T2	20010828	JP 1998-535034	19980206
NZ 337131	A	20010831	NZ 1998-337131	19980206
MX 9907290	A	20000531	MX 1999-7290	19990806
NZ 507275	A	20011130	NZ 2000-507275	20001003
NZ 507276	A	20020201	NZ 2000-507276	20001003
AU 771024	B2	20040311	AU 2000-72261	20001214
AU 771434	B2	20040325	AU 2000-72260	20001214

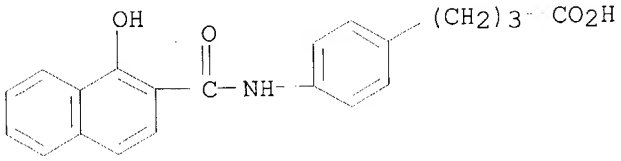
PRIORITY APPLN. INFO.:
US 1997-796334 A 19970207
US 1997-796335 A 19970207
US 1997-796336 A 19970207
US 1997-796337 A 19970207
US 1997-796338 A 19970207

US 1997-796339	A	19970207
US 1997-796340	A	19970207
US 1997-796341	A	19970207
US 1997-797100	A	19970207
US 1997-797813	A	19970207
US 1997-797816	A	19970207
US 1997-797817	A	19970207
US 1997-797820	A	19970207
AU 1998-62756	A3	19980206
CA 1998-2279331	A3	19980206
EP 1998-905042	A3	19980206
EP 1999-117292	A3	19980206
JP 1998-535034	A3	19980206
NZ 1998-337131	A1	19980206
WO 1998-US2619	W	19980206

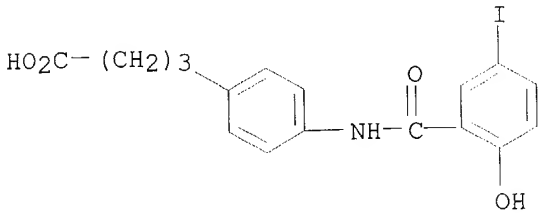
AB Carrier compds. and compns. which are useful in the delivery of active agents are provided. Methods of administration and preparation are provided as well. Standard methods of preparation are mentioned for the 193 carrier compds.
listed, which primarily are N-(fatty acid) benzamide derivs. Examples are listed for the delivery of parathyroid hormone, recombinant human growth hormone, interferon and the evaluation of heparin in rats.

IT **209961-45-5P 209961-75-1P 209961-80-8P**
209961-83-1P 209961-85-3P 209962-03-8P
209962-04-9P 209962-15-2P 209962-17-4P
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of benzamide fatty acid derivs. for delivering active agents)

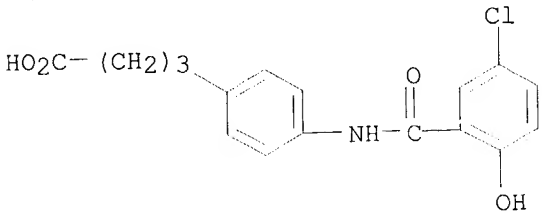
RN 209961-45-5 HCAPLUS
CN Benzenebutanoic acid, 4-[[(1-hydroxy-2-naphthalenyl)carbonyl]amino]- (9CI) (CA INDEX NAME)



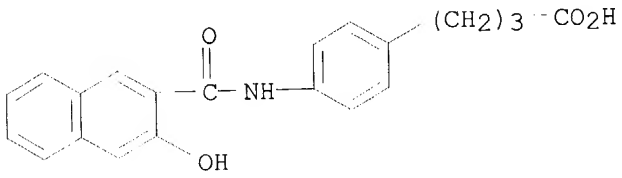
RN 209961-75-1 HCAPLUS
CN Benzenebutanoic acid, 4-[(2-hydroxy-5-iodobenzoyl)amino]- (9CI) (CA INDEX NAME)



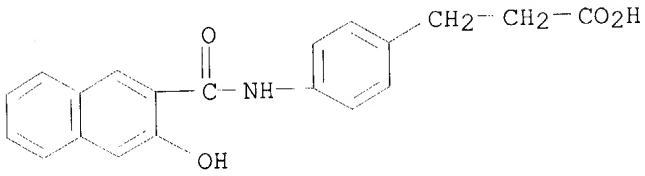
RN 209961-80-8 HCAPLUS
CN Benzenebutanoic acid, 4-[(5-chloro-2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)



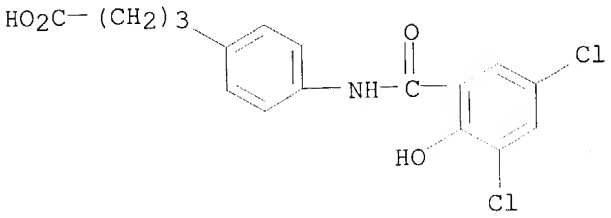
RN 209961-83-1 HCAPLUS
CN Benzenebutanoic acid, 4-[[(3-hydroxy-2-naphthalenyl)carbonyl]amino]- (9CI) (CA INDEX NAME)



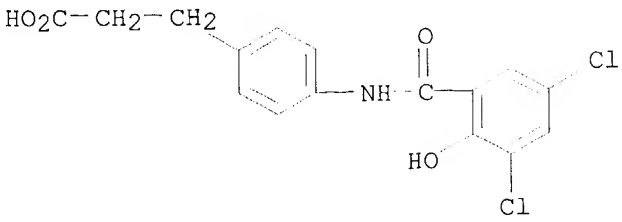
RN 209961-85-3 HCAPLUS
CN Benzenepropanoic acid, 4-[[(3-hydroxy-2-naphthalenyl)carbonyl]amino]- (9CI) (CA INDEX NAME)



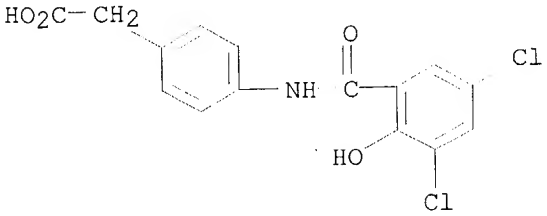
RN 209962-03-8 HCAPLUS
CN Benzenebutanoic acid, 4-[(3,5-dichloro-2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)



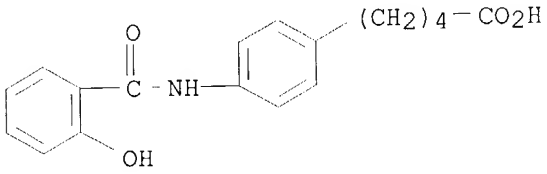
RN 209962-04-9 HCAPLUS
CN Benzenepropanoic acid, 4-[(3,5-dichloro-2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)



RN 209962-15-2 HCAPLUS
CN Benzeneacetic acid, 4-[(3,5-dichloro-2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)



RN 209962-17-4 HCAPLUS
CN Benzenepentanoic acid, 4-[(2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 22 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:430107 HCAPLUS
DOCUMENT NUMBER: 129:113525
TITLE: Compounds and compositions for delivering active agents
INVENTOR(S): Leone-Bay, Andrea; Wang, Eric; Sarubbi, Donald J.; Leipold, Harry
PATENT ASSIGNEE(S): Emisphere Technologies, Inc., USA
SOURCE: U.S., 35 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 30
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5773647	A	19980630	US 1997-796337	19970207
CA 2319672	AA	19980813	CA 1998-2319672	19980206

CA 2319680	AA	19980813	CA 1998-2319680 19980206
WO 9834632	A1	19980813	WO 1998-US2619 19980206
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, US, US, US, US, US, US, US, US, US, US, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM		
RW:	GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG		
AU 9862756	A1	19980826	AU 1998-62756 19980206
AU 738735	B2	20010927	
EP 993831	A2	20000419	EP 1999-117292 19980206
EP 993831	A3	20010502	
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI		
EP 1015008	A1	20000705	EP 1998-905042 19980206
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI		
EP 1093819	A2	20010425	EP 2000-122704 19980206
EP 1093819	A3	20030514	
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI		
JP 2001131090	A2	20010515	JP 2000-311231 19980206
JP 2001139494	A2	20010522	JP 2000-311230 19980206
JP 2001513080	T2	20010828	JP 1998-535034 19980206
NZ 337131	A	20010831	NZ 1998-337131 19980206
MX 9907290	A	20000531	MX 1999-7290 19990806
NZ 507275	A	20011130	NZ 2000-507275 20001003
NZ 507276	A	20020201	NZ 2000-507276 20001003
AU 771024	B2	20040311	AU 2000-72261 20001214
AU 771434	B2	20040325	AU 2000-72260 20001214

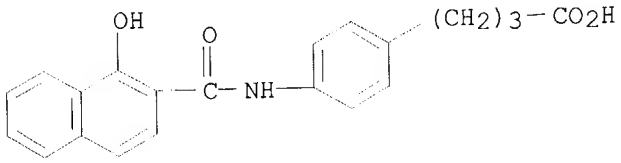
PRIORITY APPLN. INFO.:

US 1997-796334	A	19970207
US 1997-796335	A	19970207
US 1997-796336	A	19970207
US 1997-796337	A	19970207
US 1997-796338	A	19970207
US 1997-796339	A	19970207
US 1997-796340	A	19970207
US 1997-796341	A	19970207
US 1997-797100	A	19970207
US 1997-797813	A	19970207
US 1997-797816	A	19970207
US 1997-797817	A	19970207
US 1997-797820	A	19970207
AU 1998-62756	A3	19980206
CA 1998-2279331	A3	19980206
EP 1998-905042	A3	19980206
EP 1999-117292	A3	19980206
JP 1998-535034	A3	19980206
NZ 1998-337131	A1	19980206
WO 1998-US2619	W	19980206

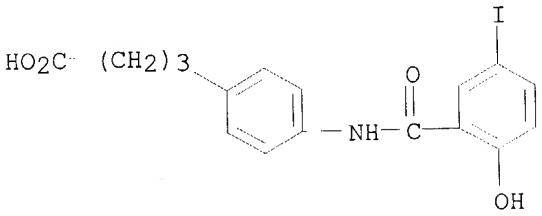
AB Carrier compds. and compns. therewith which are useful in the delivery of active agents are provided. Methods of administration and preparation are provided as well. Standard methods of preparation are mentioned for the 193 carrier compds. listed, which primarily are N-(fatty acid) benzamide derivs. Examples are listed for the delivery of parathyroid hormone, recombinant human growth hormone, interferon and the evaluation of heparin in rats.

IT **209961-45-5P 209961-75-1P 209961-80-8P**
209961-83-1P 209961-85-3P 209962-03-8P
209962-04-9P 209962-15-2P 209962-17-4P
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of benzamide fatty acids for delivering active agents)

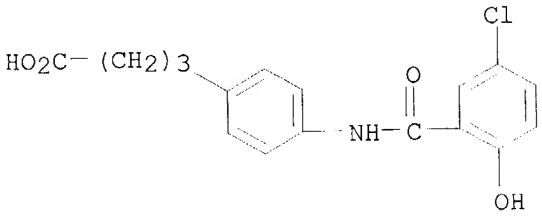
RN 209961-45-5 HCAPLUS
CN Benzenebutanoic acid, 4-[[(1-hydroxy-2-naphthalenyl)carbonyl]amino]- (9CI) (CA INDEX NAME)



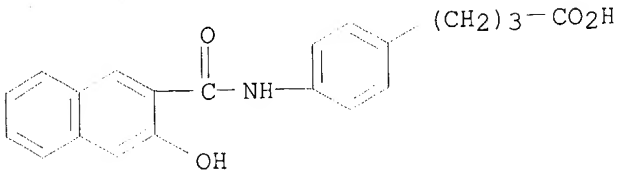
RN 209961-75-1 HCAPLUS
CN Benzenebutanoic acid, 4-[(2-hydroxy-5-iodobenzoyl)amino]- (9CI) (CA INDEX NAME)



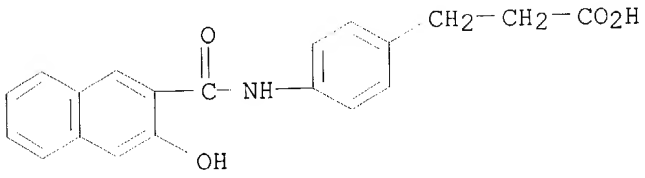
RN 209961-80-8 HCAPLUS
CN Benzenebutanoic acid, 4-[(5-chloro-2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)



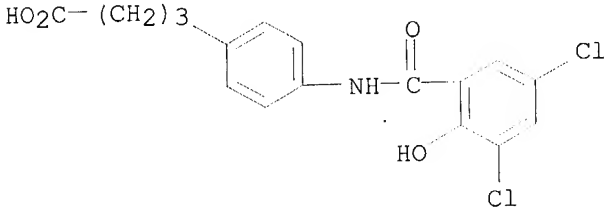
RN 209961-83-1 HCAPLUS
CN Benzenebutanoic acid, 4-[[(3-hydroxy-2-naphthalenyl)carbonyl]amino]- (9CI) (CA INDEX NAME)



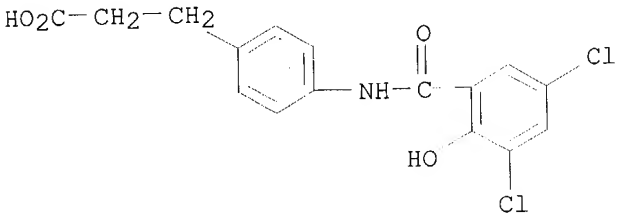
RN 209961-85-3 HCAPLUS
CN Benzenepropanoic acid, 4-[[(3-hydroxy-2-naphthalenyl)carbonyl]amino]- (9CI) (CA INDEX NAME)



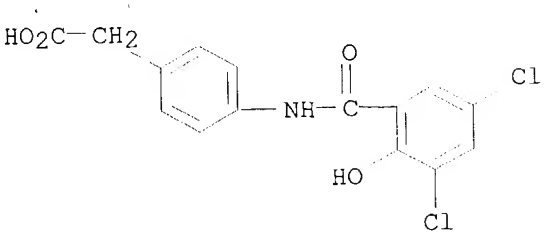
RN 209962-03-8 HCAPLUS
CN Benzenebutanoic acid, 4-[(3,5-dichloro-2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)



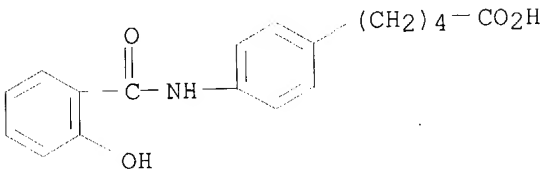
RN 209962-04-9 HCAPLUS
CN Benzenepropanoic acid, 4-[(3,5-dichloro-2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)



RN 209962-15-2 HCAPLUS
CN Benzeneacetic acid, 4-[(3,5-dichloro-2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)



RN 209962-17-4 HCAPLUS
CN Benzenepentanoic acid, 4-[(2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 23 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:344628 HCAPLUS
DOCUMENT NUMBER: 129:36449
TITLE: Methods and compositions using derivatized amino acids for inducing oral tolerance in mammals
INVENTOR(S): Haas, Susan; Milstein, Sam J.
PATENT ASSIGNEE(S): Emisphere Technologies, Inc., USA; Haas, Susan; Milstein, Sam J.
SOURCE: PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9821951	A1	19980528	WO 1997-US14676	19970820
W: CA, IL, JP, MX, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2243643	AA	19980528	CA 1997-2243643	19970820
EP 886471	A1	19981230	EP 1997-939468	19970820
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
US 6391303	B1	20020521	US 1999-101921	19990503
US 2002061311	A1	20020523	US 2001-17076	20011214

PRIORITY APPLN. INFO.:

US 1996-31356P	P	19961118
US 1997-49691P	P	19970616
WO 1997-US14676	W	19970820
US 1999-101921	A1	19990503

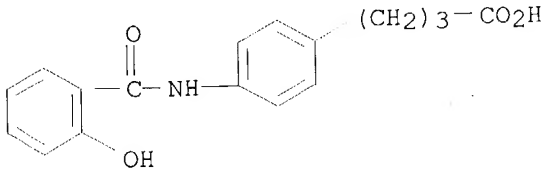
OTHER SOURCE(S): MARPAT 129:36449

AB Methods and pharmaceutical formulations are provided for orally delivering an antigen to induce tolerance. The antigen is combined with derivatized amino acids or salts thereof. The induction of oral tolerance may be

applied clin. for the prevention or treatment of autoimmune diseases and clin. allergic hypersensitivities, and for the prevention of allograft rejection.

IT **177653-18-8**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(derivatized amino acids for inducing oral tolerance)

RN 177653-18-8 HCAPLUS
CN Benzenebutanoic acid, 4-[(2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)



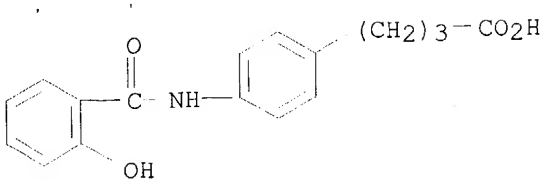
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 24 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:313029 HCAPLUS
DOCUMENT NUMBER: 129:8535
TITLE: Novel delivery agents for mucosal immunization
AUTHOR(S): Haas, S.; Meleski, D.; Kutzy, T.; Lercara, C.; O'toole, D.; Leipold, H.
CORPORATE SOURCE: Emisphere Technologies, Inc., Hawthorne, NY, 10532-2152, USA
SOURCE: S.T.P. Pharma Sciences (1998), 8(1), 59-65
CODEN: STSSE5; ISSN: 1157-1489
PUBLISHER: Editions de Sante
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Soluble, low mol. weight delivery agents provide a novel approach to the mucosal delivery of antigens. These compds. are easily synthesized by conventional chemical methods, and may be dissolved directly in an antigen solution/suspension for convenient administration. Antigen-specific secretory IgA (fecal and salivary) and systemic responses (circulating anti-ovalbumin isotypes and antigen-specific delayed-type hypersensitivity) were induced by dosing ovalbumin together with various delivery agents either orally or colonically. The data suggest that delivery agents facilitate transport of antigenically intact ovalbumin through the mucosa of both the upper and lower gastro-intestinal tracts. The possible mechanism of action and potential applications are discussed.

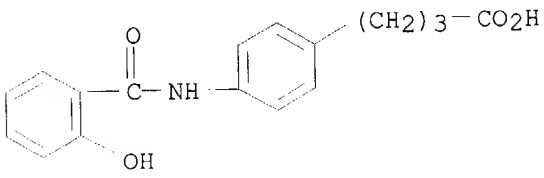
IT **177653-18-8**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(delivery agents for mucosal immunization)

RN 177653-18-8 HCAPLUS
CN Benzenebutanoic acid, 4-[(2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 25 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:790387 HCAPLUS
DOCUMENT NUMBER: 128:106314
TITLE: Acylated non-α-amino acids as novel agents for the oral delivery of heparin sodium, USP
AUTHOR(S): Leone-Bay, Andrea; Paton, Duncan R.; Variano, Bruce; Leipold, Harry; Rivera, Theresa; Miura-Fraboni, Judy; Baughman, Robert A.; Santiago, Noemi
CORPORATE SOURCE: Hawthorne, 15 Skyline Drive, Emisphere Technologies, Inc., New York, 10532, USA
SOURCE: Journal of Controlled Release (1998), 50(1-3), 41-49
CODEN: JCREEC; ISSN: 0168-3659
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Ten N-acylated, non-α-amino acids were prepared as oral delivery agents and used to demonstrate the oral delivery of heparin in vivo in rats and primates. Following the oral administration of solns. containing a combination of heparin and a delivery agent to rats or primates, significant plasma heparin concns. were evidenced by APTT and anti-Factor Xa assays. The estimated pharmacodynamic equivalence for an oral dosing solution containing heparin and a delivery agent is 39 in primates. In vitro expts. based on heparin affinity chromatog. or heparin/methylene blue complexation were also performed to begin investigation of the mechanism by which these compds. facilitate heparin oral delivery. Results of in vitro studies suggest that absorption of the drug across the gastrointestinal membrane is the result of a noncovalent interaction between heparin and the delivery agent.
IT **177653-18-8**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(acylated non-α-amino acids for delivery of heparin)
RN 177653-18-8 HCAPLUS
CN Benzenebutanoic acid, 4-[(2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 26 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1997:672238 HCAPLUS
DOCUMENT NUMBER: 127:322800
TITLE: Modified amino acids for drug delivery
INVENTOR(S): Leone-Bay, Andrea
PATENT ASSIGNEE(S): Emishphere Technologies, Inc., USA; Leone-Bay, Andrea
SOURCE: PCT Int. Appl., 64 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 30
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9736480	A1	19971009	WO 1997-US5128	19970318
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 6090958	A	20000718	US 1997-797816	19970207
AU 9725956	A1	19971022	AU 1997-25956	19970318
AU 771024	B2	20040311	AU 2000-72261	20001214
AU 771434	B2	20040325	AU 2000-72260	20001214

PRIORITY APPLN. INFO.:

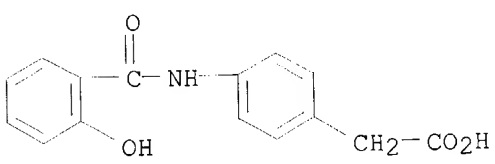
US 1996-17902	A1	19960329
US 1996-17902P	P	19960329
WO 1997-US5128	A2	19970318
AU 1998-62756	A3	19980206

OTHER SOURCE(S): MARPAT 127:322800

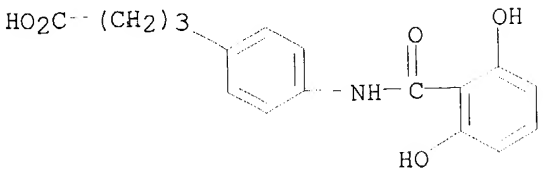
AB Modified amino acid compds. useful in the delivery of active agents are provided. E.g., 2HOC6H4CONH(CH2)7CO2H was prepared from 8-aminocaprylic acid and O-acetylsalicyloyl chloride. Also examples were give of a nol. of delivery agents enhancement of recombinant human growth hormone bioavailability administered s.c. in rats.

IT **61126-74-7P 177653-30-4P 177653-62-2P**
177653-64-4P 183990-74-1P
RL: BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(modified amino acids for drug delivery)

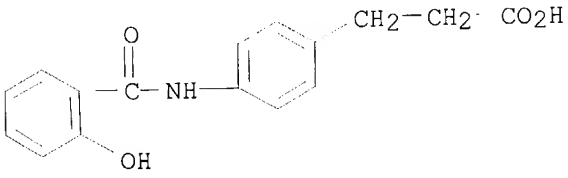
RN 61126-74-7 HCAPLUS
CN Benzeneacetic acid, 4-[(2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)



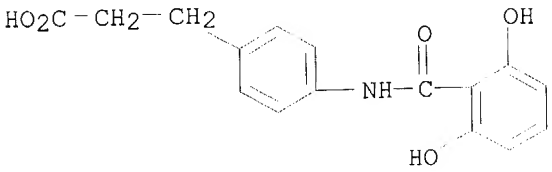
RN 177653-30-4 HCAPLUS
CN Benzenebutanoic acid, 4-[(2,6-dihydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)



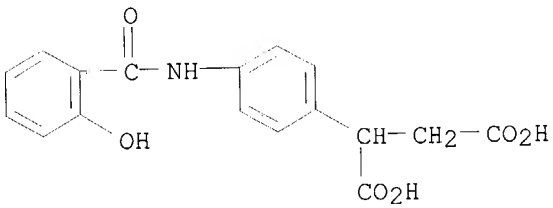
RN 177653-62-2 HCAPLUS
CN Benzenepropanoic acid, 4-[(2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)



RN 177653-64-4 HCAPLUS
CN Benzenepropanoic acid, 4-[(2,6-dihydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)



RN 183990-74-1 HCAPLUS
CN Butanedioic acid, [4-[(2-hydroxybenzoyl)amino]phenyl]- (9CI) (CA INDEX NAME)



L17 ANSWER 27 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:527636 HCAPLUS
DOCUMENT NUMBER: 127:152958
TITLE: Modified amino acid carriers, their preparation, and compositions containing them for delivering active agents
INVENTOR(S): Leone-Bay, Andrea; Paton, Duncan R.; Ho, Koc-Kan; DeMorin, Frenel
PATENT ASSIGNEE(S): Emisphere Technologies, Inc., USA
SOURCE: U.S., 22 pp., Cont.-in-part of U.S. Ser. No. 231,622.
CODEN: USXXAM

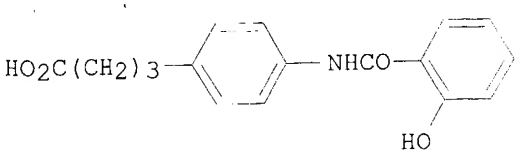
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 30
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5643957	A	19970701	US 1994-335148	19941025
US 5451410	A	19950919	US 1993-51019	19930422
US 5792451	A	19980811	US 1994-205511	19940302
US 5629020	A	19970513	US 1994-231622	19940422
CA 2203033	AA	19960502	CA 1995-2203033	19951016
WO 9612473	A1	19960502	WO 1995-US13527	19951016
W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9539633	A1	19960515	AU 1995-39633	19951016
AU 711887	B2	19991021		
EP 783299	A1	19970716	EP 1995-937558	19951016
EP 783299	B1	20030910		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
BR 9510168	A	19971014	BR 1995-10168	19951016
HU 77759	A2	19980728	HU 1998-903	19951016
JP 10507762	T2	19980728	JP 1995-514062	19951016
AT 249422	E	20030915	AT 1995-937558	19951016
ES 2207655	T3	20040601	ES 1995-937558	19951016
US 5955503	A	19990921	US 1997-795833	19970206
US 6100298	A	20000808	US 1997-795837	19970206
NO 9701889	A	19970623	NO 1997-1889	19970424
FI 9701776	A	19970425	FI 1997-1776	19970425
US 2001003001	A1	20010607	US 2000-730156	20001205
AU 771024	B2	20040311	AU 2000-72261	20001214
AU 771434	B2	20040325	AU 2000-72260	20001214
US 2002120009	A1	20020829	US 2002-90012	20020221
US 6663887	B2	20031216		
US 2004068013	A1	20040408	US 2003-677906	20031001

PRIORITY APPLN. INFO.:

US 1993-51019	A2	19930422
US 1994-205511	A2	19940302
US 1994-231622	A2	19940422
WO 1994-US4560	A2	19940422
US 1994-335148	A	19941025
WO 1995-US13527	W	19951016
US 1997-795837	A1	19970206
AU 1998-62756	A3	19980206
US 1999-346970	A1	19990702
US 2000-730156	A1	20001205
US 2002-90012	A1	20020221

OTHER SOURCE(S): MARPAT 127:152958
GI

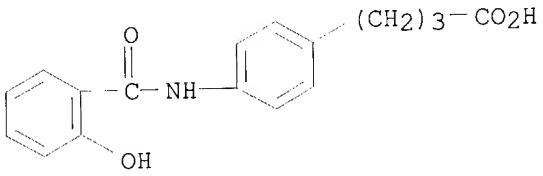


I

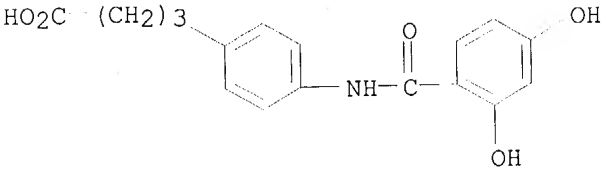
AB Modified amino acid compds. useful in the delivery of active agents (peptides, carbohydrates, antigens, monoclonal antibodies, hormones, pesticides, etc.) are provided. Methods of administration and preparation are also provided. The effect of a composition containing e.g. interferon-α2 and e.g. I (preparation given) on the serum interferon level was determined

IT **177653-18-8P 177653-26-8P**
RL: AGR (Agricultural use); BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(modified amino acid carrier preparation and compns. containing them for delivering active agents)

RN 177653-18-8 HCAPLUS
CN Benzenebutanoic acid, 4-[(2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)

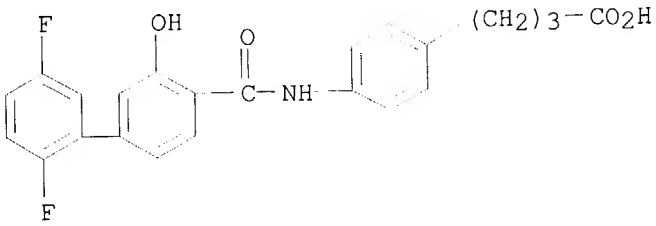


RN 177653-26-8 HCAPLUS
CN Benzenebutanoic acid, 4-[(2,4-dihydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)

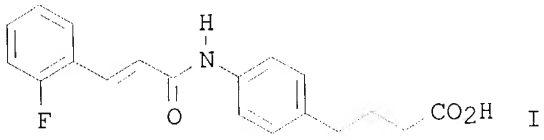


IT **178558-94-6**
RL: AGR (Agricultural use); BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(modified amino acid carrier preparation and compns. containing them for delivering active agents)

RN 178558-94-6 HCAPLUS
CN Benzenebutanoic acid, 4-[[(2',5'-difluoro-3-hydroxy[1,1'-biphenyl]-4-yl)carbonyl]amino]- (9CI) (CA INDEX NAME)



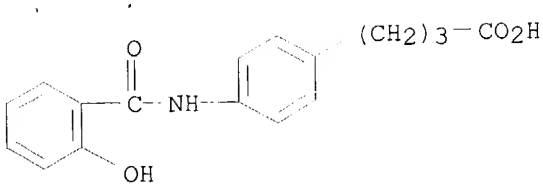
L17 ANSWER 28 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:146141 HCAPLUS
DOCUMENT NUMBER: 126:263909
TITLE: Solution phase preparation of highly pure amide mixtures via in-situ chlorotrimethylsilane protection and activation
AUTHOR(S): Ho, Koc-Kan; Wang, Nai Fang; Lercara, Christine; O'Toole, Doris C.; Achan, Douglas M.; Vuocolo, Edmund A.; Leone-Bay, Andrea
CORPORATE SOURCE: Emisphere Technol. Inc., Hawthorne, NY, 10532, USA
SOURCE: Synthetic Communications (1997), 27(5), 883-895
CODEN: SYNCAV; ISSN: 0039-7911
PUBLISHER: Dekker
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 126:263909
GI



AB Coupling of 4-(4-aminophenyl)butyric acid with acyl halides in both organic and aqueous media were found to produce large amount of oligomeric materials. By using an in situ chlorotrimethylsilane protection/activation procedure, these oligomers were suppressed completely and the desired 4-(4-acylaminophenyl)butyric acids, e.g. I, were obtained in good yield and high purity. The method was also extended to a parallel synthesis of a three component mixture 1H-NMR of the mixture indicated that each component was formed in a nearly stoichiometric quantity.

IT **177653-18-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of (acylamino)benzenebutanoates via protection and activation with chlorotrimethylsilane)

RN 177653-18-8 HCAPLUS
CN Benzenebutanoic acid, 4-[(2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 29 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:87 HCAPLUS
DOCUMENT NUMBER: 126:31174
TITLE: Preparation of modified amino acid compounds for delivering active agents
INVENTOR(S): Leone-Bay, Andrea; Ho, Koc-Kan; Sarubbi, Donald J.; Milstein, Sam J.; Press, Jeffery Bruce
PATENT ASSIGNEE(S): Emisphere Technologies, Inc., USA; Leone-Bay, Andrea; Ho, Koc-Kan; Sarubbi, Donald, J.; Milstein, Sam, J.; Press, Jeffery, Bruce
SOURCE: PCT Int. Appl., 86 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 30
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9630036	A1	19961003	WO 1996-US4580	19960401
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA				
US 5650386	A	19970722	US 1995-414654	19950331
CA 2214323	AA	19961003	CA 1996-2214323	19960401
AU 9656629	A1	19961016	AU 1996-56629	19960401
AU 712222	B2	19991104		
EP 817643	A1	19980114	EP 1996-913778	19960401
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI				
BR 9604880	A	19980519	BR 1996-4880	19960401
JP 2002506418	T2	20020226	JP 1996-529751	19960401
RU 2203268	C2	20030427	RU 1997-118224	19960401
JP 2003313157	A2	20031106	JP 2003-140962	19960401
US 5965121	A	19991012	US 1997-798023	19970206
US 5989539	A	19991123	US 1997-798032	19970206
US 6001347	A	19991214	US 1997-798031	19970206
FI 9703828	A	19970929	FI 1997-3828	19970929
NO 9704495	A	19971128	NO 1997-4495	19970929
US 2001023240	A1	20010920	US 1999-305506	19990505
US 6428780	B2	20020806		
US 6346242	B1	20020212	US 2000-499958	20000208
AU 771024	B2	20040311	AU 2000-72261	20001214
AU 771434	B2	20040325	AU 2000-72260	20001214
US 2003045579	A1	20030306	US 2001-38426	20011019

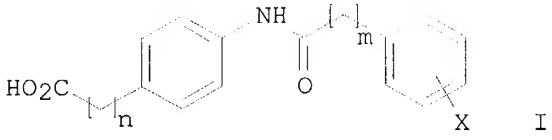
US 6623731	B2	20030923			
US 2003078302	A1	20030424	US 2002-142009		20020508
US 6699467	B2	20040302			
US 2004110839	A1	20040610	US 2003-623142		20030718

PRIORITY APPLN. INFO.:

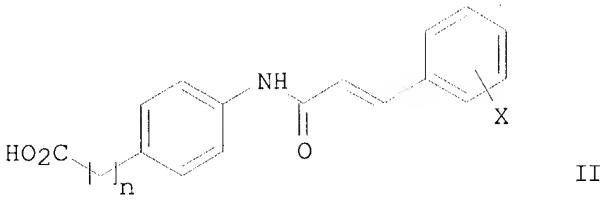
US 1995-414654	A2	19950331
US 1995-3111P	P	19950901
US 1996-17902P	P	19960329
JP 1996-529751	A3	19960401
WO 1996-US4580	W	19960401
US 1997-798031	A1	19970206
AU 1998-62756	A3	19980206
US 1999-305506	A1	19990505
US 2000-499958	A1	20000208
US 2001-38426	A1	20011019

OTHER SOURCE(S): MARPAT 126:31174

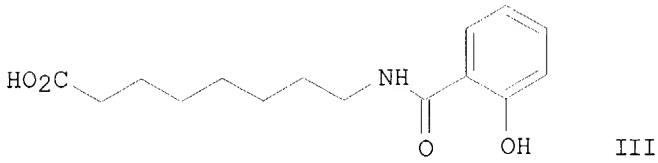
GI



I



II



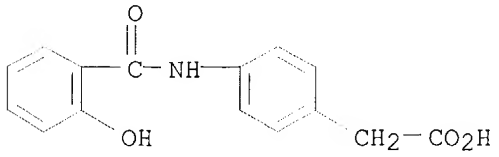
III

AB Modified amino acid compds. [I (n = 0-3; m = 0-4; X = H, halo, OH, etc.), II (n = 0-3; X = 2-F, 3-MeO, 4-Me, etc.), etc.], useful in the delivery of active agents such as, e.g., human growth hormone, interferon, heparin, calcitonin, parathyroid hormone, were prepared Thus, reaction of 8-aminocaprylic acid with O-acetylsalicyloyl chloride in the presence of 2M aqueous NaOH afforded 57% III which was mixed with recombinant growth hormone (rhGH) in a phosphate buffer solution at pH 7-8 and administered orally to rats at 25 mg/kg of carrier and at 1 mg/kg of rhGH. The mean peak serum level of compound III was 60.92 ng/mL as compared to < 10 ng/mL for control.

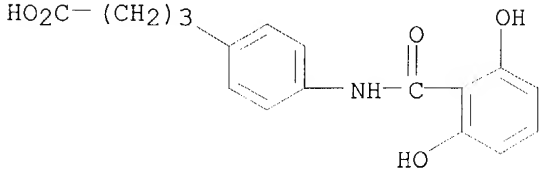
IT **61126-74-7P 177653-30-4P 177653-62-2P**
177653-64-4P 183990-68-3P 183990-74-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of modified amino acid compds. for delivering active agents)

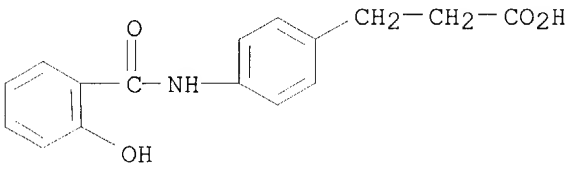
RN 61126-74-7 HCAPLUS
CN Benzeneacetic acid, 4-[(2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)



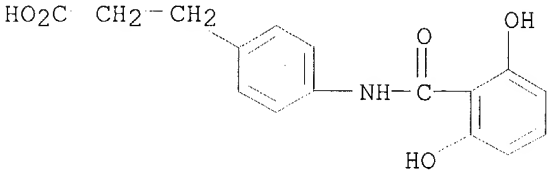
RN 177653-30-4 HCAPLUS
CN Benzenebutanoic acid, 4-[(2,6-dihydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)



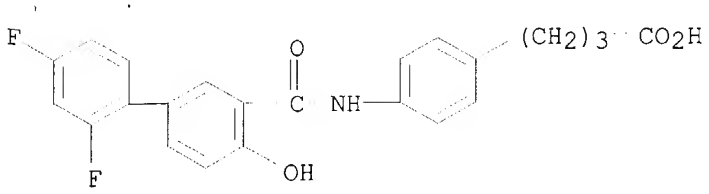
RN 177653-62-2 HCAPLUS
CN Benzenepropanoic acid, 4-[(2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)



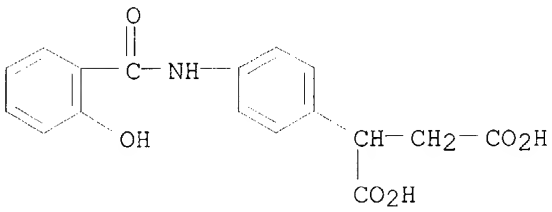
RN 177653-64-4 HCAPLUS
CN Benzenepropanoic acid, 4-[(2,6-dihydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)



RN 183990-68-3 HCAPLUS
CN Benzenebutanoic acid, 4-[[(2',4'-difluoro-4-hydroxy[1,1'-biphenyl]-3-yl)carbonyl]amino]- (9CI) (CA INDEX NAME)



RN 183990-74-1 HCAPLUS
CN Butanedioic acid, [4-[(2-hydroxybenzoyl)amino]phenyl]- (9CI) (CA INDEX NAME)

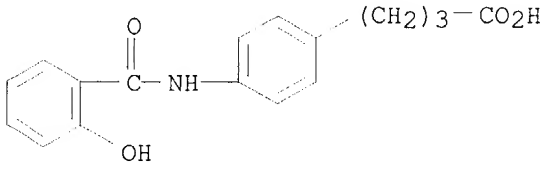


L17 ANSWER 30 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1996:562097 HCAPLUS
DOCUMENT NUMBER: 125:256974
TITLE: Interaction of heparin with aromatic compounds: analysis of heparin affinity chromatography, equilibrium dialysis and circular dichroism spectroscopy
AUTHOR(S): Liao, Jun; Zhao, Ruifeng; Milstein, Sam; Ottenbrite, Raphael M.
CORPORATE SOURCE: High Technology Materials Center, Virginia Commonwealth University, Richmond, VA, 23284-2006, USA
SOURCE: Polymer Preprints (American Chemical Society, Division of Polymer Chemistry) (1996), 37(2), 157-158
CODEN: ACPPAY; ISSN: 0032-3934
PUBLISHER: American Chemical Society, Division of Polymer Chemistry
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Clin. heparin (I) has to be administered via injection since the mol. structure, along with its biol. activities, is sensitive to the components in the gastrointestinal tract. Therefore, to develop an oral delivery system for I is important. A number of low mol. weight aromatic compds. were found to facilitate transport of heparin and protein drugs across the gastrointestinal epithelium and facilitated the oral delivery of these drugs to rats and primates. It was further revealed that these aromatic compds. interact with protein drugs, such as rhGH (recombinant human growth hormone), rhIFn (recombinant human α-interferon), insulin, and that the interaction induces a reversible denaturalization of the native conformation of the drugs. The study of the interaction of heparin with the aromatic compds. E452, E445, and E352, was studied using I affinity chromatog., equilibrium dialysis and CD spectroscopy.

IT **177653-18-8**, E 352
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(interaction of heparin with aromatic compds.: anal. of heparin affinity chromatog., equilibrium dialysis and CD spectroscopy)
RN 177653-18-8 HCAPLUS
CN Benzenebutanoic acid, 4-[(2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)



L17 ANSWER 31 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1996:425385 HCAPLUS
DOCUMENT NUMBER: 125:96071
TITLE: Modified amino acids as absorption enhancers for delivering active agents
INVENTOR(S): Leone-Bay, Andrea; Paton, Duncan R.; Ho, Kok-Kan; Demorin, Frenel
PATENT ASSIGNEE(S): Emisphere Technologies, Inc., USA
SOURCE: PCT Int. Appl., 57 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 30
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9612473	A1	19960502	WO 1995-US13527	19951016
W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5643957	A	19970701	US 1994-335148	19941025
AU 9539633	A1	19960515	AU 1995-39633	19951016
AU 711887	B2	19991021		
EP 783299	A1	19970716	EP 1995-937558	19951016
EP 783299	B1	20030910		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
BR 9510168	A	19971014	BR 1995-10168	19951016
JP 10507762	T2	19980728	JP 1995-514062	19951016
AT 249422	E	20030915	AT 1995-937558	19951016
NO 9701889	A	19970623	NO 1997-1889	19970424
FI 9701776	A	19970425	FI 1997-1776	19970425
AU 771024	B2	20040311	AU 2000-72261	20001214
AU 771434	B2	20040325	AU 2000-72260	20001214

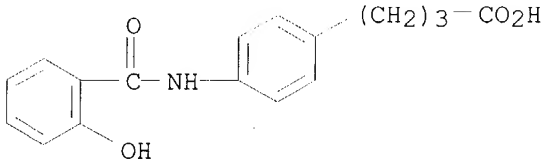
PRIORITY APPLN. INFO.:
US 1994-335148 A 19941025
US 1993-51019 A2 19930422
US 1994-205511 A2 19940302
US 1994-231622 A2 19940422
WO 1995-US13527 W 19951016
AU 1998-62756 A3 19980206

AB Modified amino acid compds. as absorption enhancers are useful in the

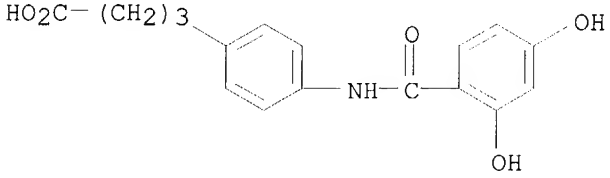
delivery of active agents. These compound are used as carriers to facilitate the delivery of a cargo to a target. Thus, 47.00 g acetylsalicyloyl chloride was added to a mixture of 50.00 g 4-(4-aminophenyl)butyric acid in 300 mL of 2M aqueous sodium hydroxide and the reaction was stirred at 25° for 2 h, then it was acidified with aqueous HCl to obtain a precipitate which was separated and washed to give 31.89 g 4-(2-hydroxyphenylcarbonylamino)p-phenylbutanoic acid (I). I was mixed with interferon α-2 (II) in Tris-HCl buffer pH = 7-8 and was orally administered to rats at a rate of 300 mg I/kg and 1000 μg II/kg. The mean peak serum level of II was 8213 as compared to 688 ng/mL for controls.

IT **177653-18-8P 177653-26-8P 178558-94-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(modified amino acids as absorption enhancers for delivering active agents)

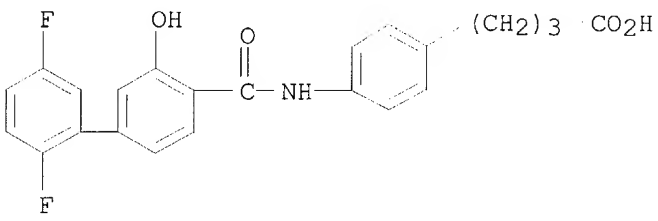
RN 177653-18-8 HCAPLUS
CN Benzenebutanoic acid, 4-[(2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)



RN 177653-26-8 HCAPLUS
CN Benzenebutanoic acid, 4-[(2,4-dihydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)



RN 178558-94-6 HCAPLUS
CN Benzenebutanoic acid, 4-[[(2',5'-difluoro-3-hydroxy[1,1'-biphenyl]-4-yl)carbonyl]amino]- (9CI) (CA INDEX NAME)



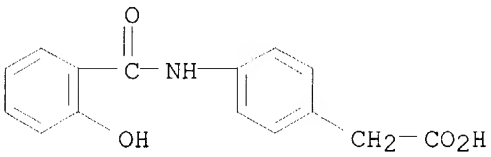
L17 ANSWER 32 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1996:326446 HCAPLUS

DOCUMENT NUMBER: 125:18819
TITLE: 4-[4-[(2-Hydroxybenzoyl)amino]phenyl]butyric Acid as a Novel Oral Delivery Agent for Recombinant Human Growth Hormone
AUTHOR(S): Leone-Bay, Andrea; Ho, Koc-Kan; Agarwal, Rajesh; Baughman, Robert A.; Chaudhary, Kiran; DeMorin, Frenel; Genoble, Lise; McInnes, Campbell; Lercara, Christine; et al.
CORPORATE SOURCE: Emisphere Technologies Inc., Hawthorne, NY, 10532, USA
SOURCE: Journal of Medicinal Chemistry (1996), 39(13), 2571-2578
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

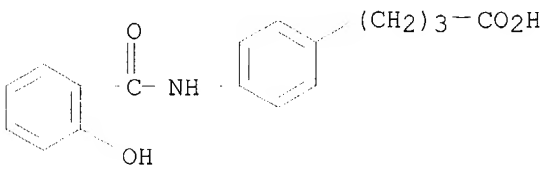
AB A series of N-acetylated, non-α, aromatic aminocarboxylic acids was prepared and shown to promote the absorption of recombinant human growth hormone (rhGH) from the gastrointestinal tract. Seventy compds. in this family were tested in vivo in rats. Of the compds. tested, 4-[4-[(2-hydroxybenzoyl)amino]phenyl]butyric acid was identified as a preclin. candidate and was used to demonstrate the oral delivery of rhGH in primates. A significant pos. correlation was found between the relative log k' of the delivery agents, as determined by HPLC on an immobilized artificial membrane (IAM) column, and serum rhGH concns. following oral or colonic dosing in rats. Structure-activity relationships were also developed on the basis of electronic effects and hydrogen-bonding characteristics of the aromatic amide substituents.

IT **61126-74-7 177653-18-8 177653-26-8 177653-30-4 177653-62-2 177653-64-4**
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hydroxybenzoylaminophenylbutyrate as oral vehicle for human growth hormone)

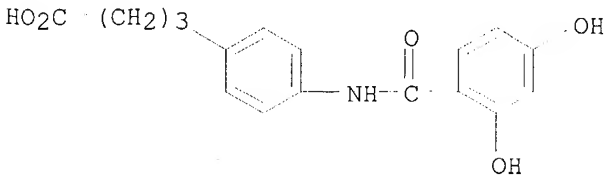
RN 61126-74-7 HCAPLUS
CN Benzeneacetic acid, 4-[(2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)



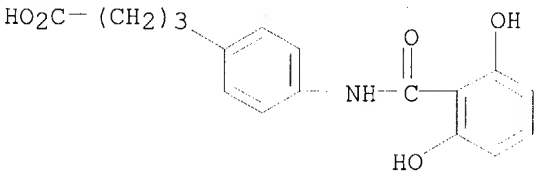
RN 177653-18-8 HCAPLUS
CN Benzenebutanoic acid, 4-[(2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)



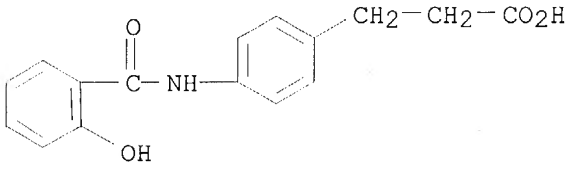
RN 177653-26-8 HCAPLUS
CN Benzenebutanoic acid, 4-[(2,4-dihydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)



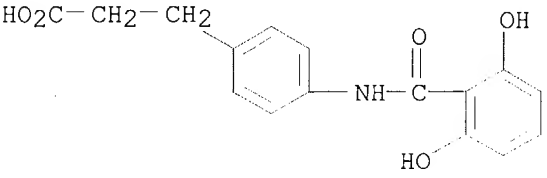
RN 177653-30-4 HCAPLUS
CN Benzenebutanoic acid, 4-[(2,6-dihydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)



RN 177653-62-2 HCAPLUS
CN Benzenepropanoic acid, 4-[(2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)

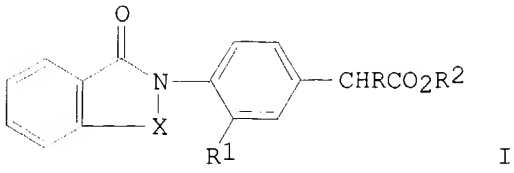


RN 177653-64-4 HCAPLUS
CN Benzenepropanoic acid, 4-[(2,6-dihydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)



L17 ANSWER 33 OF 33 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1977:5402 HCAPLUS
DOCUMENT NUMBER: 86:5402
TITLE: Synthesis of quinazolinone and benzoxazinone acids and study of their antiinflammatory properties
AUTHOR(S): Picciola, G.
CORPORATE SOURCE: Lab. Ric., Maggioni e C. S.p.A., Milan, Italy
SOURCE: Farmaco, Edizione Scientifica (1976), 31(9), 655-64
CODEN: FRPSAX; ISSN: 0430-0920
DOCUMENT TYPE: Journal
LANGUAGE: Italian

GI

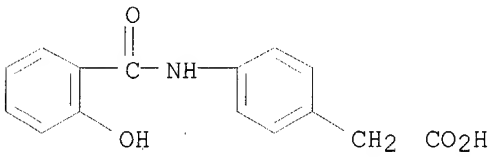


I

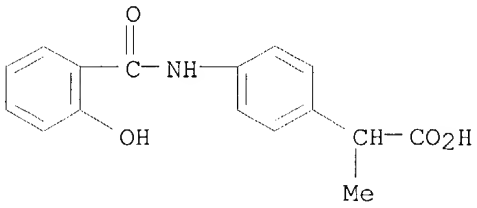
AB Quinazolinylphenylacetic acids I (X = N:CH, N:CMe, N:CPr; R = H, Me; R1 = H, Cl; R2 = H, Et), I (X = NHCH2, NHCHMe; R = H, Me; R1 = H; R2 = H, Et), benzoxazinephenylacetic acids I (X = OCH2; R = H, Me; R1 = H, Cl; R2 = H, Et), and 3,4-R1(2-HOC6H4CONH)C6H3CHRCO2R2 (R = H, Me; R1 = H, Cl; R2 = H, Et) were prepared by various methods. None of the compds. showed any antiinflammatory activity.

IT **61126-74-7P 61126-76-9P 61126-78-1P 61126-80-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

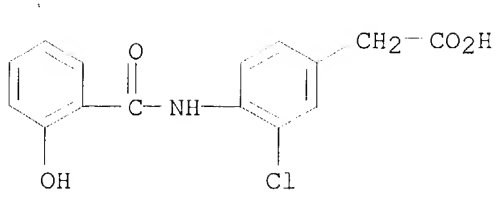
RN 61126-74-7 HCAPLUS
CN Benzeneacetic acid, 4-[(2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)



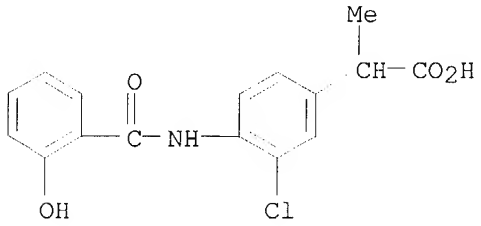
RN 61126-76-9 HCAPLUS
CN Benzeneacetic acid, 4-[(2-hydroxybenzoyl)amino]-α-methyl- (9CI) (CA INDEX NAME)



RN 61126-78-1 HCAPLUS
CN Benzeneacetic acid, 3-chloro-4-[(2-hydroxybenzoyl)amino]- (9CI) (CA INDEX NAME)



RN 61126-80-5 HCAPLUS
CN Benzeneacetic acid, 3-chloro-4-[(2-hydroxybenzoyl)amino]-α-methyl-
(9CI) (CA INDEX NAME)



=> d ibib abs hitstr l25 1-37

L25 ANSWER 1 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:964132 HCAPLUS
DOCUMENT NUMBER: 138:29141
TITLE: Compound and composition for **delivering** biologically **active agents**, such as parathyroid hormone
INVENTOR(S): **Leone-Bay, Andrea**
PATENT ASSIGNEE(S): Emisphere Technologies, Inc., USA
SOURCE: PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002100338	A2	20021219	WO 2002-US18236	20020607
WO 2002100338	A3	20040212		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-297117P P 20010608

AB Compds. and compns. for the **delivery** of biol. **active agents**, i.e., a protein, polypeptide, peptide, hormone, polysaccharide, mucopolysaccharide, carbohydrate, or lipid, are provided. These compds. are well suited for forming non-covalent mixts. with **active agents** for oral, pulmonary, and other routes of administration. Methods for the preparation and administration of such compns. are provided as well. For example, a **delivery** agent, 9-(4-hydroxybenzoylamino)nonanoic acid (I), was prepared from 1.17 equivalent of 8-aminononanoic acid and 1.00 equivalent of 4-hydroxybenzoyl chloride and used for oral/intracolonic **delivery** of human parathyroid hormone residues 1-34 (PTH) by mixing I with a PTH stock solution (typically having a concentration of 5 mg PTH/mL) and diluting to the desired volume (usually 3.0 mL).

L25 ANSWER 2 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:526048 HCAPLUS
DOCUMENT NUMBER: 135:122313
TITLE: Synthesis of benzoylaminophenyl derivatives for **delivering active agents**
INVENTOR(S): Boyd, Maria Aurora P.; **Leone-Bay, Andrea**; O'Toole, Doris C.
PATENT ASSIGNEE(S): Emisphere Technologies, Inc., USA
SOURCE: PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

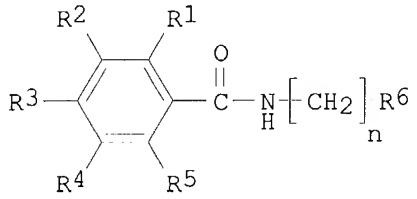
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001051454	A1	20010719	WO 2001-US1274	20010112
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1246792	A1	20021009	EP 2001-908609	20010112
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003528822	T2	20030930	JP 2001-551836	20010112
US 2003149296	A1	20030807	US 2002-181275	20020805

PRIORITY APPLN. INFO.:

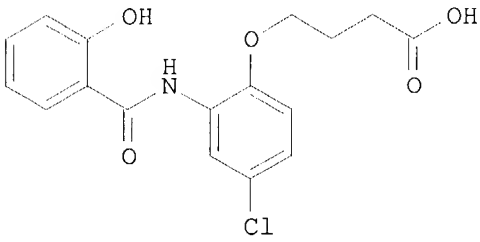
US 2000-175947P	P	20000113
US 2000-194421P	P	20000404
US 2000-202210P	P	20000505
WO 2001-US1274	W	20010112

OTHER SOURCE(S): MARPAT 135:122313

GI



I



II

AB Title compds. I [R1-5 = H, halo, OH, OMe, alkyl, NH2, NHMe, NMe2 or NO2; n = 0 - 4; R6 = C6H4-O-R7-COOH optionally substituted with OH, OMe, alkyl, NH2, NHMe, NMe2, NO2, where R7 = alkyl] were prepared for use as **delivery** compds. for **active agents**. Eleven synthetic examples were provided. 2-Amino-4-chlorophenol was O-alkylated with Et 4-bromo butyrate. The intermediate ester was N-acylated with acetylsalicyloyl chloride and saponified to give II. Formulations of **delivery** compds./actives (e.g. insulin, parathyroid hormone, interferon, etc.), their (oral) administration and determination of serum concentration over time were described. A formulation containing 200 mg/kg II and 0.5 mg/kg insulin administered orally (Sprague-Dawley rats) gave a mean peak serum

insulin concentration of 110.59 ± 11.84 pg/mL. Oral administration of insulin without the drug **delivery** agent revealed no measurable levels of serum insulin.

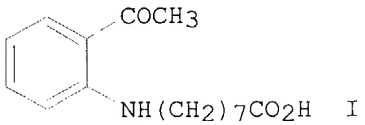
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 3 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:338308 HCAPLUS
DOCUMENT NUMBER: 134:357556
TITLE: Phenyl amine carboxylic acid compounds and compositions for **delivering active agents**
INVENTOR(S): **Leone-Bay, Andrea**; Kraft, Kelly; Boyd, Maria A. P.
PATENT ASSIGNEE(S): Emisphere Technologies, Inc., USA
SOURCE: PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001032130	A2	20010510	WO 2000-US41960	20001106
WO 2001032130	A3	20020314		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2001026223	A5	20010514	AU 2001-26223	20001106
EP 1226109	A2	20020731	EP 2000-989761	20001106
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004501057	T2	20040115	JP 2001-534338	20001106
ZA 2002002365	A	20021025	ZA 2002-2365	20020325

PRIORITY APPLN. INFO.:
US 1999-163806P P 19991105
US 2000-231836P P 20000906
US 2000-237233P P 20001002
WO 2000-US41960 W 20001106

OTHER SOURCE(S): MARPAT 134:357556
GI



I

AB Phenylaminecarboxylic acid compds. and compns. for the **delivery** of **active agents** are provided. E.g., I was prepared and used for oral **delivery** of drugs such as insulin.

L25 ANSWER 4 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:297631 HCAPLUS
DOCUMENT NUMBER: 134:316090
TITLE: **Active agent** transport systems
INVENTOR(S): **Milstein, Sam J.**; **Leone-Bay, Andrea** ; **Sarubbi, Donald J.**; Leipold, Harry
PATENT ASSIGNEE(S): Emisphere Technologies, Inc., USA
SOURCE: U.S., 73 pp., Cont.-in-part of U.S. 6,099,856.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 30
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6221367	B1	20010424	US 1997-939939	19970929
US 5443841	A	19950822	US 1992-920346	19920727
US 5451410	A	19950919	US 1993-51019	19930422
US 5578323	A	19961126	US 1993-76803	19930614
US 5447728	A	19950905	US 1993-168776	19931216
US 5792451	A	19980811	US 1994-205511	19940302
US 5541155	A	19960730	US 1994-231623	19940422
US 5629020	A	19970513	US 1994-231622	19940422
US 5693338	A	19971202	US 1994-315200	19940929
US 6331318	B1	20011218	US 1994-316404	19940930
ZA 9408342	A	19950622	ZA 1994-8342	19941024
US 5714167	A	19980203	US 1994-328932	19941025
US 6099856	A	20000808	US 1996-763183	19961210
US 6344213	B1	20020205	US 1997-820694	19970318
CA 2304951	AA	19990408	CA 1998-2304951	19980929
WO 9916427	A1	19990408	WO 1998-US20548	19980929
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9895136	A1	19990423	AU 1998-95136	19980929
AU 735693	B2	20010712		
EP 1021169	A1	20000726	EP 1998-948597	19980929
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001517694	T2	20011009	JP 2000-513565	19980929
AU 771024	B2	20040311	AU 2000-72261	20001214
AU 771434	B2	20040325	AU 2000-72260	20001214
US 2001039258	A1	20011108	US 2001-760307	20010111
US 2002127202	A1	20020912	US 2001-5511	20011107
US 2002155993	A1	20021024	US 2002-125836	20020419
US 6663898	B2	20031216		
US 2003198658	A1	20031023	US 2003-443713	20030521

PRIORITY APPLN. INFO.:
US 1992-898909 B2 19920615
US 1992-920346 A2 19920727
US 1993-51019 B2 19930422
US 1993-76803 A2 19930614
US 1993-143571 B2 19931026
US 1993-168776 A2 19931216

US	1994-205511	A2 19940302
US	1994-205511	A2 19940302
US	1994-231622	A2 19940422
US	1994-231623	B2 19940422
WO	1994-US4560	A2 19940422
US	1994-315200	A2 19940929
US	1994-316404	A2 19940930
US	1994-328932	A2 19941025
US	1996-17902P	P 19960329
US	1996-763183	A2 19961210
US	1997-820694	A2 19970318
US	1997-939939	A 19970929
AU	1998-62756	A3 19980206
WO	1998-US20548	W 19980929
US	2001-929530	A1 20010813
US	2002-125836	A1 20020419

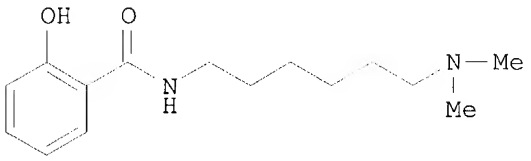
AB Methods for transporting a biol. **active agent** across a cellular membrane or a lipid bilayer includes the steps of: (a) providing a biol. **active agent** which can exist in a native conformational state, a denatured conformational state, and an intermediate conformational state which is reversible to the native state and which is conformationally between the native and denatured states; (b) exposing the biol. **active agent** to a complexing perturbant to reversibly transform the biol. **active agent** to the intermediate state and to form a transportable supramol. complex; and (c) exposing the membrane or bilayer to the supramol. complex, to transport the biol. **active agent** across the membrane or bilayer. The perturbant has a mol. weight between about 150 and about 600 daltons, and contains at least one hydrophilic moiety and at least one hydrophobic moiety. The supramol. complex comprises the perturbant non-covalently bound or complexed with the biol. **active agent**. In the present invention, the biol. **active agent** does not form a microsphere after interacting with the perturbant. A method for preparing an orally administrable biol. **active agent** comprising steps (a) and (b) above is also provided as are oral **delivery** compns. Addnl., mimetics and methods for preparing mimetics are contemplated. One example gives penetrant phenylsulfonyl-p-aminobenzoic acid effect on α-interferon.

REFERENCE COUNT: 721 THERE ARE 721 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 5 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:608713 HCAPLUS
DOCUMENT NUMBER: 133:213157
TITLE: Aromatic amides for **delivering active agents**
INVENTOR(S): Tang, Pingwah; **Leone-Bay, Andrea**; Gschneidner, David
PATENT ASSIGNEE(S): Emisphere Technologies, Inc., USA
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2000050386 A1 20000831 WO 2000-US4830 20000225
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
EP 1163209 A1 20011219 EP 2000-911975 20000225
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO
JP 2002537372 T2 20021105 JP 2000-600970 20000225
US 2002040061 A1 20020404 US 2001-939511 20010824
US 6646162 B2 20031111
PRIORITY APPLN. INFO.: US 1999-121850P P 19990226
WO 2000-US4830 W 20000225
OTHER SOURCE(S): MARPAT 133:213157
GI



I

AB Amides such as I are used for the **delivery** of **active agents** such as growth hormones. I was prepared from carsalam and 6-dimethylamino-1-hexanol, Ph3P, and diisopropyl azodicarboxylate in THF. Examples were given showing oral **delivery** of salmon calcitonin, low mol. wt heparin and human growth hormone with the addition of I.
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 6 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:547374 HCAPLUS
DOCUMENT NUMBER: 133:155438
TITLE: **Active agent** transport systems comprising amino acids
INVENTOR(S): **Milstein, Sam J.**; Barantsevitch, Evgueni; **Leone-Bay, Andrea**; Wang, Nai Fang; **Sarubbi, Donald J.**; Santiago, Noemi B.
PATENT ASSIGNEE(S): Emisphere Technologies, Inc., USA
SOURCE: U.S., 71 pp., Cont.-in-part of U.S. 5,714,167.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 30
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6099856	A	20000808	US 1996-763183	19961210
US 5443841	A	19950822	US 1992-920346	19920727
US 5451410	A	19950919	US 1993-51019	19930422

US 5578323	A	19961126	US 1993-76803	19930614	
US 5447728	A	19950905	US 1993-168776	19931216	
US 5792451	A	19980811	US 1994-205511	19940302	
US 5541155	A	19960730	US 1994-231623	19940422	
US 5629020	A	19970513	US 1994-231622	19940422	
US 5693338	A	19971202	US 1994-315200	19940929	
US 6331318	B1	20011218	US 1994-316404	19940930	
ZA 9408342	A	19950622	ZA 1994-8342	19941024	
US 5714167	A	19980203	US 1994-328932	19941025	
US 6221367	B1	20010424	US 1997-939939	19970929	
WO 9825589	A1	19980618	WO 1997-US23545	19971209	
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
AU 9855322	A1	19980703	AU 1998-55322	19971209	
AU 771024	B2	20040311	AU 2000-72261	20001214	
AU 771434	B2	20040325	AU 2000-72260	20001214	
US 2001039258	A1	20011108	US 2001-760307	20010111	
US 2002155993	A1	20021024	US 2002-125836	20020419	
US 6663898	B2	20031216			
US 2003133953	A1	20030717	US 2002-255237	20020925	
US 2003198658	A1	20031023	US 2003-443713	20030521	

PRIORITY APPLN. INFO.:

US 1992-898909	B2	19920615
US 1992-920346	A2	19920727
US 1993-51019	A2	19930422
US 1993-76803	A2	19930614
US 1993-143571	B2	19931026
US 1993-168776	A2	19931216
US 1994-205511	A2	19940302
US 1994-231622	A2	19940422
US 1994-231623	A2	19940422
WO 1994-US4560	A2	19940422
US 1994-315200	A2	19940929
US 1994-316404	A2	19940930
US 1994-328932	A2	19941025
US 1996-17902P	P	19960329
US 1996-763183	A2	19961210
US 1997-820694	A2	19970318
US 1997-939939	A1	19970929
WO 1997-US23545	W	19971209
AU 1998-62756	A3	19980206
US 1999-420200	A1	19991018
US 2001-929530	A1	20010813
US 2002-125836	A1	20020419

OTHER SOURCE(S): MARPAT 133:155438

AB Methods for transporting a biol. **active agent** across a cellular membrane or a lipid bilayer. A first method includes the steps of: (a) providing a biol. **active agent** which can exist in a native conformational state, a denatured conformational state, and an intermediate conformational state which is reversible to the native state and which is conformationally between the native and denatured states; (b) exposing the biol. **active agent** to a complexing perturbant to reversibly transform the biol. **active agent** to the intermediate state and to form a transportable supramol. complex; and (c) exposing the membrane or bilayer to the

supramol. complex, to transport the biol. **active agent** across the membrane or bilayer. The perturbant has a mol. weight between about 150 and about 600 Daltons, and contains at least one hydrophilic moiety and at least one hydrophobic moiety. The supramol. complex comprises the perturbant non-covalently bound or complexed with the biol. **active agent**. In the present invention, the biol. **active agent** does not form a microsphere after interacting with the perturbant. A method for preparing an orally administrable biol. **active agent** comprising steps (a) and (b) above is also provided as are oral **delivery** compns. Addnl., mimetics and methods for preparing mimetics are contemplated. Native gradient gels were run with 647 mg/mL of α-interferon, and increasing amts. (10-500 mg/mL) of perturbant (a mixture of L-Valine, L-Leucine, L-phenylalanine, L-lysine and L-arginine modified with benzenesulfonylchloride). As the amount of perturbant added was increased in each subsequent lane relative to a fixed concentration of α-interferon, the α-interferon migrated to a lower, rather than a higher, mol. weight This indicated that the α-interferon structure was changing, because if the structure was not changing, there would be a shift towards higher mol. weight as perturbant complexes with the **active agent** . Oral administration of above α-interferon and perturbant to rats at 500 μg/kg showed significant blood level of α-interferon as compared with controls with no perturbant.

REFERENCE COUNT: 734 THERE ARE 734 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 7 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:492070 HCAPLUS
DOCUMENT NUMBER: 133:109955
TITLE: Amino acid derivatives and compositions therewith for **delivering active agents**
INVENTOR(S): **Leone-Bay, Andrea; Ho, Koc-kan; Sarubbi, Donald J.**; Leipold, Harry R.
PATENT ASSIGNEE(S): Emisphere Technologies, Inc., USA
SOURCE: U.S., 44 pp., Cont.-in-part of PCT 9736480. CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 30
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6090958	A	20000718	US 1997-797816	19970207
WO 9736480	A1	19971009	WO 1997-US5128	19970318
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2319672	AA	19980813	CA 1998-2319672	19980206
CA 2319680	AA	19980813	CA 1998-2319680	19980206
WO 9834632	A1	19980813	WO 1998-US2619	19980206
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ,				

PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG,
US, US, US, US, US, US, US, US, US, US, US, US, US, UZ, VN, YU,
ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI,
FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM,
GA, GN, ML, MR, NE, SN, TD, TG

AU 9862756	A1	19980826	AU 1998-62756	19980206	
AU 738735	B2	20010927			
EP 993831	A2	20000419	EP 1999-117292	19980206	
EP 993831	A3	20010502			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
EP 1015008	A1	20000705	EP 1998-905042	19980206	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
EP 1093819	A2	20010425	EP 2000-122704	19980206	
EP 1093819	A3	20030514			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
JP 2001131090	A2	20010515	JP 2000-311231	19980206	
JP 2001139494	A2	20010522	JP 2000-311230	19980206	
JP 2001513080	T2	20010828	JP 1998-535034	19980206	
NZ 337131	A	20010831	NZ 1998-337131	19980206	
MX 9907290	A	20000531	MX 1999-7290	19990806	
NZ 507275	A	20011130	NZ 2000-507275	20001003	
NZ 507276	A	20020201	NZ 2000-507276	20001003	
AU 771024	B2	20040311	AU 2000-72261	20001214	
AU 771434	B2	20040325	AU 2000-72260	20001214	

PRIORITY APPLN. INFO.:

US 1996-17902P	P	19960329
WO 1997-US5128	A2	19970318
US 1996-17902	A1	19960329
US 1997-796334	A	19970207
US 1997-796335	A	19970207
US 1997-796336	A	19970207
US 1997-796337	A	19970207
US 1997-796338	A	19970207
US 1997-796339	A	19970207
US 1997-796340	A	19970207
US 1997-796341	A	19970207
US 1997-797100	A	19970207
US 1997-797813	A	19970207
US 1997-797816	A	19970207
US 1997-797817	A	19970207
US 1997-797820	A	19970207
AU 1998-62756	A3	19980206
CA 1998-2279331	A3	19980206
EP 1998-905042	A3	19980206
EP 1999-117292	A3	19980206
JP 1998-535034	A3	19980206
NZ 1998-337131	A1	19980206
WO 1998-US2619	W	19980206

AB Carrier compds., especially amino acid derivs., and compns. therewith which are useful in the **delivery** of **active agents**, e.g. peptides, mucopolysaccharides, carbohydrates, and lipids, are provided. Methods of administration and preparation are provided as well. An intracolonic dosing composition containing parathyroid hormone 25 μg/kg, 4-[4-(phenoxyacetyl)aminophenyl]butyric acid as carrier 100 mg/kg in 25% aqueous propylene glycol was prepared

L25 ANSWER 8 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2000:475505 HCAPLUS
DOCUMENT NUMBER: 133:109945
TITLE: Polymeric **delivery** agents comprising a polymer conjugated to a modified amino acid or derivative thereof
INVENTOR(S): **Milstein, Sam J.**; Barantsevitch, Eugene N.; Wang, Nai Fang; Liao, Jun; Smart, John E.; Conticello, Richard D.; Ottenbrite, Raphael M.
PATENT ASSIGNEE(S): Emisphere Technologies, Inc., USA; Virginia Commonwealth University
SOURCE: PCT Int. Appl., 91 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000040203	A2	20000713	WO 2000-US476	20000107
WO 2000040203	A3	20001214		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2358463	AA	20000713	CA 2000-2358463	20000107
EP 1146860	A2	20011024	EP 2000-914419	20000107
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 2000008590	A	20011030	BR 2000-8590	20000107
JP 2002534363	T2	20021015	JP 2000-591961	20000107
NZ 512581	A	20021220	NZ 2000-512581	20000107
ZA 2001005213	A	20020717	ZA 2001-5213	20010625
US 6627228	B1	20030930	US 2001-889005	20011009
US 2003232085	A1	20031218	US 2003-447608	20030528

PRIORITY APPLN. INFO.: US 1999-115273P P 19990108
WO 2000-US476 W 20000107
US 2001-889005 A1 20011009

AB Polymeric **delivery** agents comprising a polymer conjugated to a modified amino acid or derivative thereof, **delivery** agent compds. and compns. comprising them which are useful in the **delivery** of **active agents** are provided. Poly(N-acryloxysuccinimide) was conjugated with N-(5-aminomethylsalicyloyl)-8-aminocaprylic acid (preparation given). Oral and intracolonic **delivery** composition comprising human growth hormone and above conjugate was administered to rats. At a dose of 200 mg/kg conjugate, the actual amount of **delivery** agent dosed was 20 mg/kg. With such a concentration of **delivery** agent complexed with polymer there was evidence of systemic **delivery**.

L25 ANSWER 9 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:117018 HCAPLUS
DOCUMENT NUMBER: 132:151567
TITLE: Preparation of arylamidoalkylcarboxylic acids and compositions for **delivering active**

agents.

INVENTOR(S): Gschneidner, David; **Leone-Bay, Andrea**; Wang, Eric; Errigo, Lynn; Kraft, Kelly; Moye-Sherman, Destardi; **Ho, Koc-Kan**; Press, Jeffrey Bruce; Wang, Nai Fang

PATENT ASSIGNEE(S): Emisphere Technologies, Inc., USA

SOURCE: PCT Int. Appl., 53 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000007979	A2	20000217	WO 1999-US17974	19990806
WO 2000007979	A3	20000518		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2339765	AA	20000217	CA 1999-2339765	19990806
AU 9954711	A1	20000228	AU 1999-54711	19990806
EP 1102742	A2	20010530	EP 1999-940967	19990806
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 9912975	A	20010925	BR 1999-12975	19990806
TR 200100366	T2	20011121	TR 2001-20010036619990806	
JP 2002522413	T2	20020723	JP 2000-563614	19990806
NZ 509410	A	20030829	NZ 1999-509410	19990806
ZA 2001000470	A	20010820	ZA 2001-470	20010117

PRIORITY APPLN. INFO.:

US 1998-95778P	P	19980807
US 1998-98500P	P	19980831
US 1998-108366P	P	19981113
US 1999-119207P	P	19990205
WO 1999-US17974	W	19990806

AB 135 Title compds. are claimed. Thus, Me azeloyl chloride was added dropwise to 2-amino-p-cresol in aqueous NaOH at 0° to give a residue which was stirred with aqueous NaOH in THF to give 4-HO-5-MeC6H3NHCO(CH2)7CO2H. Title compds. at 100-300 mg/kg with parathyroid hormone at 25-200 μg orally or intracolonically in rats gave peak serum parathyroid hormone levels of 5-1459.71 pg/mL.

L25 ANSWER 10 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2000:98355 HCAPLUS

DOCUMENT NUMBER: 132:141984

TITLE: Pulmonary **delivery** of **active agents**

INVENTOR(S): **Milstein, Sam J.**; Smart, John E.; **Sarubbi, Donald J.**; Carozza, Monica; Flanders, Elizabeth; O'Toole, Doris; **Leone-Bay, Andrea**; Gschneidner, David

PATENT ASSIGNEE(S): Emisphere Technologies, Inc., USA

SOURCE: PCT Int. Appl., 47 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000006184	A1	20000210	WO 1999-US16957	19990727
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2338358	AA	20000210	CA 1999-2338358	19990727
CA 2338419	AA	20000210	CA 1999-2338419	19990727
WO 2000006534	A1	20000210	WO 1999-US17090	19990727
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9953210	A1	20000221	AU 1999-53210	19990727
AU 745290	B2	20020321		
AU 9953237	A1	20000221	AU 1999-53237	19990727
AU 751612	B2	20020822		
EP 1100522	A1	20010523	EP 1999-938806	19990727
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
EP 1100771	A1	20010523	EP 1999-938842	19990727
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
TR 200100922	T2	20010921	TR 2001-20010092219990727	
BR 9912694	A	20020102	BR 1999-12694	19990727
JP 2002521455	T2	20020716	JP 2000-562038	19990727
NZ 509239	A	20021025	NZ 1999-509239	19990727
JP 2003517438	T2	20030527	JP 2000-562341	19990727
NZ 509238	A	20030725	NZ 1999-509238	19990727
ZA 2001000227	A	20010807	ZA 2001-227	20010109
ZA 2001000226	A	20010904	ZA 2001-226	20010109
US 6642411	B1	20031104	US 2001-744862	20010419
US 6440929	B1	20020827	US 2001-744777	20010426
US 2003072740	A1	20030417	US 2002-172582	20020614
US 6693073	B2	20040217		
US 2003225300	A1	20031204	US 2003-600413	20030620

PRIORITY APPLN. INFO.:
US 1998-94267P P 19980727
US 1998-104466P P 19981016
WO 1999-US16957 W 19990727
WO 1999-US17090 W 19990727
US 2001-744862 A1 20010419
US 2001-744777 A1 20010426

OTHER SOURCE(S): MARPAT 132:141984

AB Methods of administration of **active agents** via the

pulmonary route are provided. Thus, sodium 2-(4-(N-salicyloyl)aminophenyl)propionate was prepared and 16 mg/kg this compound was mixed with 0.05 mg/kg porcine insulin and administered to rats by lung-spray-IT instillation. The AUC of the formulation wa higher than that without any carrier added.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 11 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:233788 HCAPLUS
DOCUMENT NUMBER: 130:287040
TITLE: **Delivery** of biologically **active agents** across cell membranes involving active transport systems
INVENTOR(S): **Milstein, Sam J.**; **Leone-Bay, Andrea**; **Sarubbi, Donald J.**; Leipold, Harry
PATENT ASSIGNEE(S): Emisphere Technologies, Inc., USA
SOURCE: PCT Int. Appl., 164 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 30
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9916427	A1	19990408	WO 1998-US20548	19980929
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6221367	B1	20010424	US 1997-939939	19970929
CA 2304951	AA	19990408	CA 1998-2304951	19980929
AU 9895136	A1	19990423	AU 1998-95136	19980929
AU 735693	B2	20010712		
EP 1021169	A1	20000726	EP 1998-948597	19980929
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001517694	T2	20011009	JP 2000-513565	19980929
AU 771024	B2	20040311	AU 2000-72261	20001214
AU 771434	B2	20040325	AU 2000-72260	20001214

PRIORITY APPLN. INFO.:

US 1997-939939	A1	19970929
US 1992-898909	B2	19920615
US 1992-920346	A2	19920727
US 1993-51019	B2	19930422
US 1993-76803	A2	19930614
US 1993-143571	B2	19931026
US 1993-168776	A2	19931216
US 1994-205511	A2	19940302
US 1994-231622	A2	19940422
US 1994-231623	B2	19940422
WO 1994-US4560	A2	19940422
US 1994-315200	A2	19940929
US 1994-316404	A2	19940930
US 1994-328932	A2	19941025
US 1996-17902P	P	19960329

US 1996-763183 A2 19961210
US 1997-820694 A2 19970318
AU 1998-62756 A3 19980206
WO 1998-US20548 W 19980929

OTHER SOURCE(S): MARPAT 130:287040

AB Methods for transporting a biol. **active agent** across a cellular membrane or a lipid bilayer are disclosed. A first method includes the steps of: (a) providing a biol. **active agent** which can exist in a native conformational state, a denatured conformational state, and an intermediate conformational state which is reversible to the native state and which is conformationally between the native and denatured states; (b) exposing the biol. **active agent** to a complexing perturbant to reversibly transform the biol. **active agent** to the intermediate state and to form a transportable supramol. complex; and (c) exposing the membrane or bilayer to the supramol. complex, to transport the biol. **active agent** across the membrane or bilayer. The perturbant has a mol. weight between about 150 and about 600 daltons, and contains at least one hydrophilic moiety and at least one hydrophobic moiety. The supramol. complex comprises the perturbant non-covalently bound or complexed with the biol. **active agent**. In the present invention, the biol. **active agent** does not form a microsphere after interacting with the perturbant. A method for preparing an orally administrable biol. **active agent** comprising steps (a) and (b) above is also provided as are oral **delivery** compns. Addnl., mimetics and methods for preparing mimetics are contemplated.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 12 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:100747 HCAPLUS
DOCUMENT NUMBER: 130:144204
TITLE: Modified amino acids as carriers for enhanced **delivery** of **active agents**
INVENTOR(S): **Leone-Bay, Andrea; Ho, Koc-kan; Sarubbi, Donald J.; Milstein, Sam J.**
PATENT ASSIGNEE(S): Emisphere Technologies, Inc., USA
SOURCE: U.S., 27 pp., Cont.-in-part of U.S. Ser. No. 414,654. CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 30
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5866536	A	19990202	US 1997-798033	19970206
US 5650386	A	19970722	US 1995-414654	19950331
CN 1190893	A	19980819	CN 1996-192998	19960401
JP 2003313157	A2	20031106	JP 2003-140962	19960401
US 6071510	A	20000606	US 1997-839094	19970423
AU 771024	B2	20040311	AU 2000-72261	20001214
AU 771434	B2	20040325	AU 2000-72260	20001214

PRIORITY APPLN. INFO.: US 1995-414654 A2 19950331
US 1995-3111P P 19950901
JP 1996-529751 A3 19960401
AU 1998-62756 A3 19980206

AB Carrier compds., compns., and dosage unit forms which are useful in the **delivery** of **active agents** are provided. The

present invention provides compds. such as 10-salicyloylaminodecanoic acid (I) for **delivery** of at least one **active agent**, including peptides, mucopolysaccharides, carbohydrates, or lipids. I prepared from 8-aminocaprylic acid and O-acetylsalicyloyl chloride was mixed with recombinant human growth hormone (rhGH) in a phosphate buffer solution The composition was orally administered to rats at I 200 mg/kg and rhGH 3 mg/kg and **delivery** was evaluated by an ELISA assay for rhGH; mean peak serum levels of rhGH was .apprx.60.92 ng/mL as compared to <0.1 ng/mL for control group received a composition without I.

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 13 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:721669 HCAPLUS
DOCUMENT NUMBER: 130:7397
TITLE: Compounds and compositions for **delivering active agents**
INVENTOR(S): **Leone-Bay, Andrea**; Gschneidner, David; Wang, Eric; **Sarubbi, Donald J.**
PATENT ASSIGNEE(S): Emisphere Technologies, Inc., USA
SOURCE: PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9849135	A1	19981105	WO 1998-US7045	19980408
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5863944	A	19990126	US 1997-846254	19970430
AU 9869590	A1	19981124	AU 1998-69590	19980408
AU 727068	B2	20001130		
EP 979225	A1	20000216	EP 1998-915393	19980408
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001524109	T2	20011127	JP 1998-547012	19980408
MX 9909632	A	20000630	MX 1999-9632	19991020

PRIORITY APPLN. INFO.: US 1997-846254 A 19970430
WO 1998-US7045 W 19980408

AB Carrier compds. and compns. which are useful in the **delivery** of **active agents** are provided, including N-2-(amino-5-fluorobenzoyl)-8-aminocaprylic acid, 4-(N-(5-fluoro-2-aminobenzoyl)-4-aminophenyl)butyric acid, and 8-(2-hydroxy-5-chloroanilinocarbonyl)octanoic acid. Methods of administration and preparation are provided as well.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 14 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:613457 HCAPLUS
DOCUMENT NUMBER: 129:250217

TITLE: Oral **delivery** system comprising modified amino acids and biologically **active agents**
INVENTOR(S): **Milstein, Sam J.**; Barantsevitch, Evgueni N.
PATENT ASSIGNEE(S): Emisphere Technologies, Inc., USA
SOURCE: U.S., 22 pp., Cont.-in-part of U.S. 5,447,728.
CODEN: USXXAM

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 30
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5811127	A	19980922	US 1996-635921	19960424
US 5443841	A	19950822	US 1992-920346	19920727
US 5451410	A	19950919	US 1993-51019	19930422
US 5578323	A	19961126	US 1993-76803	19930614
US 5447728	A	19950905	US 1993-168776	19931216
WO 9511690	A1	19950504	WO 1994-US12333	19941024
W: AM, AT, AU, BB, BG, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN				
ZA 9408342	A	19950622	ZA 1994-8342	19941024
AU 771024	B2	20040311	AU 2000-72261	20001214
AU 771434	B2	20040325	AU 2000-72260	20001214

PRIORITY APPLN. INFO.:

US 1992-898909	B2	19920615
US 1992-920346	A2	19920727
US 1993-51019	A2	19930422
US 1993-76803	A2	19930614
US 1993-143571	B2	19931026
US 1993-168776	A2	19931216
WO 1994-US12333	W	19941024
AU 1998-62756	A3	19980206

AB Modified amino acids and methods for their preparation and use as oral **delivery** systems for pharmaceutical agents are described. The modified amino acids are preparable by reacting single amino acids or mixts. of two or more kinds of amino acids with an amino modifying agent such as benzene sulfonyl chloride, benzoyl chloride, and hippuryl chloride. The modified amino acids may form encapsulating microspheres in the presence of the **active agent** under sphere-forming conditions. Alternatively, the modified amino acids may be used as a carrier by simply mixing the amino acids with the **active agent**. The preferred acylated amino acid carrier is salicyloyl-phenylalanine. The modified amino acids are particularly useful in **delivering** biol. **active agents**, e.g., desferrioxamine, insulin or cromolyn sodium, or other agents which are sensitive to the denaturing conditions of the gastrointestinal tract. Salicyloyl phenylalanine (I) was prepared from hydrogenolysis of salicyloyl phenylalanine benzyl ester (preparation given). Microspheres containing 1.5mg insulin/mL and 300 mg I/mL were prepared The sustained effect of the microspheres was shown in rats.

REFERENCE COUNT: 343 THERE ARE 343 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 15 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:548547 HCAPLUS
DOCUMENT NUMBER: 129:180147

TITLE: Compounds and compositions for **delivering active agents**
INVENTOR(S): **Leone-Bay, Andrea**; et al.
PATENT ASSIGNEE(S): Emisphere Technologies, Inc., USA
SOURCE: PCT Int. Appl., 147 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 30
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9834632	A1	19980813	WO 1998-US2619	19980206
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, US, US, US, US, US, US, US, US, US, US, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW:	GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
US 5773647	A	19980630	US 1997-796337	19970207
US 5776888	A	19980707	US 1997-796338	19970207
US 5804688	A	19980908	US 1997-796339	19970207
US 5876710	A	19990302	US 1997-796335	19970207
US 5879681	A	19990309	US 1997-796334	19970207
US 5939381	A	19990817	US 1997-796340	19970207
US 5990166	A	19991123	US 1997-797820	19970207
US 6051561	A	20000418	US 1997-797813	19970207
US 6060513	A	20000509	US 1997-797817	19970207
US 6090958	A	20000718	US 1997-797816	19970207
US 6313088	B1	20011106	US 1997-797100	19970207
US 6358504	B1	20020319	US 1997-796336	19970207
AU 9862756	A1	19980826	AU 1998-62756	19980206
AU 738735	B2	20010927		
EP 1015008	A1	20000705	EP 1998-905042	19980206
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI			
JP 2001513080	T2	20010828	JP 1998-535034	19980206
NZ 337131	A	20010831	NZ 1998-337131	19980206
MX 9907290	A	20000531	MX 1999-7290	19990806
AU 771024	B2	20040311	AU 2000-72261	20001214
AU 771434	B2	20040325	AU 2000-72260	20001214
US 2002119910	A1	20020829	US 2000-746548	20001219
US 2003008900	A1	20030109	US 2001-1731	20011031
US 6525020	B2	20030225		
US 2003235612	A1	20031225	US 2003-373582	20030224
US 2004022856	A1	20040205	US 2003-395685	20030324

PRIORITY APPLN. INFO.:

US 1997-796334 A1 19970207
US 1997-796335 A1 19970207
US 1997-796336 A1 19970207
US 1997-796337 A1 19970207
US 1997-796338 A1 19970207
US 1997-796339 A1 19970207
US 1997-796340 A1 19970207
US 1997-796341 A1 19970207
US 1997-797100 A1 19970207
US 1997-797813 A1 19970207

US 1997-797816	A1	19970207
US 1997-797817	A1	19970207
US 1997-797820	A1	19970207
US 1996-17902P	P	19960329
WO 1997-US5128	A2	19970318
AU 1998-62756	A3	19980206
EP 1999-117292	A3	19980206
WO 1998-US2619	W	19980206
US 2000-746548	B1	20001219
US 2001-1731	A1	20011031

AB Carrier compds. and compns. which are useful in the **delivery** of **active agents** are provided. The carrier compound can be an amino acid derivative, and the **active agent** can be a peptide, mucopolysaccharide, carbohydrate, or lipid. Methods of administration, including oral administration, and preparation are provided as well. For example, an oral solution contained parathyroid hormone 100 μg, 4-[4-(phenoxyacetyl)aminophenyl]butyric acid (as carrier) 400 mg, and water 1L.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 16 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:542693 HCAPLUS
DOCUMENT NUMBER: 129:180125
TITLE: Oral drug **delivery** compositions comprising modified amino acids and bioactive peptides
INVENTOR(S): **Sarubbi, Donald J.; Leone-Bay, Andrea**; Paton, Duncan R.
PATENT ASSIGNEE(S): Emisphere Technologies, Inc., USA
SOURCE: U.S., 18 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 30
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5792451	A	19980811	US 1994-205511	19940302
CA 2160693	AA	19941027	CA 1994-2160693	19940422
EP 696208	A1	19960214	EP 1994-916578	19940422
EP 696208	B1	20010822		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 08509474	T2	19961008	JP 1994-523595	19940422
EP 1025840	A2	20000809	EP 2000-103527	19940422
EP 1025840	A3	20000830		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
EP 1077070	A2	20010221	EP 2000-118505	19940422
EP 1077070	A3	20010523		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
AT 204467	E	20010915	AT 1994-916578	19940422
ES 2163444	T3	20020201	ES 1994-916578	19940422
US 5643957	A	19970701	US 1994-335148	19941025
US 5714167	A	19980203	US 1994-328932	19941025
US 5958457	A	19990928	US 1995-438644	19950510
US 5766633	A	19980616	US 1995-537888	19951023
US 6099856	A	20000808	US 1996-763183	19961210
US 5955503	A	19990921	US 1997-795833	19970206
US 6100298	A	20000808	US 1997-795837	19970206
US 6221367	B1	20010424	US 1997-939939	19970929

US 6071538	A	20000606
US 6245359	B1	20010612
US 6348207	B1	20020219
US 2001003001	A1	20010607
AU 771024	B2	20040311
AU 771434	B2	20040325
US 2002001591	A1	20020103
US 6610329	B2	20030826
US 2002052422	A1	20020502
US 6461643	B2	20021008
US 2002120009	A1	20020829
US 6663887	B2	20031216
US 2003012817	A1	20030116
US 2003133953	A1	20030717
US 2004062773	A1	20040401
US 2004068013	A1	20040408

PRIORITY APPLN. INFO.:

US 1997-940056		19970930
US 1997-941616		19970930
US 1997-941609		19970930
US 2000-730156		20001205
AU 2000-72261		20001214
AU 2000-72260		20001214
US 2001-862013		20010521
US 2001-862063		20010521
US 2002-90012		20020221
US 2002-225104		20020820
US 2002-255237		20020925
US 2003-600386		20030619
US 2003-677906		20031001
US 1992-898909	B2	19920615
US 1992-920346	A2	19920727
US 1993-51019	A	19930422
US 1993-76803	A2	19930614
US 1993-143571	B2	19931026
US 1993-168776	A2	19931216
US 1994-205511	A	19940302
EP 1994-916578	A3	19940422
US 1994-231622	A2	19940422
US 1994-231623	A2	19940422
WO 1994-US4560	W	19940422
US 1994-315200	A2	19940929
US 1994-316404	A2	19940930
US 1994-328932	A2	19941025
US 1994-335147	B2	19941025
US 1994-335148	A3	19941025
US 1995-438644	A1	19950510
US 1996-17902P	P	19960329
US 1996-763183	A2	19961210
US 1997-795837	A1	19970206
US 1997-820694	A2	19970318
AU 1998-62756	A3	19980206
US 1999-346970	A1	19990702
US 1999-346971	B1	19990702
US 1999-420200	A1	19991018
US 2000-730156	A1	20001205
US 2001-862013	A1	20010521
US 2001-862063	A1	20010521
US 2002-90012	A1	20020221

AB The present invention relates to an oral drug **delivery** system, and in particular to modified amino acid derivs. for use as a **delivery** system of sensitive agents such as bioactive peptides. The modified amino acid derivs. can form non-covalent mixts. with active biol. agents and in an alternate embodiment can releasably carry **active agents**. These mixts. are suitable for oral administration of biol. **active agents** to mammals. Methods for the preparation of such amino acids are also disclosed.

REFERENCE COUNT: 341 THERE ARE 341 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 17 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:457247 HCAPLUS
DOCUMENT NUMBER: 129:113532

TITLE: Compounds and compositions for **delivering active agents**
INVENTOR(S): **Leone-Bay, Andrea**; Wang, Eric; **Sarubbi, Donald J.**; Leipold, Harry
PATENT ASSIGNEE(S): Emisphere Technologies, Inc., USA
SOURCE: U.S., 34 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 30
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5776888	A	19980707	US 1997-796338	19970207
CA 2319672	AA	19980813	CA 1998-2319672	19980206
CA 2319680	AA	19980813	CA 1998-2319680	19980206
WO 9834632	A1	19980813	WO 1998-US2619	19980206
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, US, US, US, US, US, US, US, US, US, US, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9862756	A1	19980826	AU 1998-62756	19980206
AU 738735	B2	20010927		
EP 993831	A2	20000419	EP 1999-117292	19980206
EP 993831	A3	20010502		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
EP 1015008	A1	20000705	EP 1998-905042	19980206
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
EP 1093819	A2	20010425	EP 2000-122704	19980206
EP 1093819	A3	20030514		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001131090	A2	20010515	JP 2000-311231	19980206
JP 2001139494	A2	20010522	JP 2000-311230	19980206
JP 2001513080	T2	20010828	JP 1998-535034	19980206
NZ 337131	A	20010831	NZ 1998-337131	19980206
MX 9907290	A	20000531	MX 1999-7290	19990806
NZ 507275	A	20011130	NZ 2000-507275	20001003
NZ 507276	A	20020201	NZ 2000-507276	20001003
AU 771024	B2	20040311	AU 2000-72261	20001214
AU 771434	B2	20040325	AU 2000-72260	20001214

PRIORITY APPLN. INFO.:

US 1997-796334	A	19970207
US 1997-796335	A	19970207
US 1997-796336	A	19970207
US 1997-796337	A	19970207
US 1997-796338	A	19970207
US 1997-796339	A	19970207
US 1997-796340	A	19970207
US 1997-796341	A	19970207
US 1997-797100	A	19970207
US 1997-797813	A	19970207
US 1997-797816	A	19970207

US 1997-797817	A	19970207
US 1997-797820	A	19970207
AU 1998-62756	A3	19980206
CA 1998-2279331	A3	19980206
EP 1998-905042	A3	19980206
EP 1999-117292	A3	19980206
JP 1998-535034	A3	19980206
NZ 1998-337131	A1	19980206
WO 1998-US2619	W	19980206

AB Carrier compds. and compns. which are useful in the **delivery** of **active agents** are provided. Methods of administration and preparation are provided as well. Standard methods of preparation are mentioned for the 193 carrier compds. listed, which primarily are N-(fatty acid) benzamide derivs. Examples are listed for the **delivery** of parathyroid hormone, recombinant human growth hormone, interferon and the evaluation of heparin in rats.

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 18 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:430107 HCAPLUS
DOCUMENT NUMBER: 129:113525
TITLE: Compounds and compositions for **delivering active agents**
INVENTOR(S): **Leone-Bay, Andrea**; Wang, Eric; **Sarubbi, Donald J.**; Leipold, Harry
PATENT ASSIGNEE(S): Emisphere Technologies, Inc., USA
SOURCE: U.S., 35 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 30
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5773647	A	19980630	US 1997-796337	19970207
CA 2319672	AA	19980813	CA 1998-2319672	19980206
CA 2319680	AA	19980813	CA 1998-2319680	19980206
WO 9834632	A1	19980813	WO 1998-US2619	19980206
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, US, US, US, US, US, US, US, US, US, US, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9862756	A1	19980826	AU 1998-62756	19980206
AU 738735	B2	20010927		
EP 993831	A2	20000419	EP 1999-117292	19980206
EP 993831	A3	20010502		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
EP 1015008	A1	20000705	EP 1998-905042	19980206
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
EP 1093819	A2	20010425	EP 2000-122704	19980206

EP 1093819	A3	20030514			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
JP 2001131090	A2	20010515	JP 2000-311231		19980206
JP 2001139494	A2	20010522	JP 2000-311230		19980206
JP 2001513080	T2	20010828	JP 1998-535034		19980206
NZ 337131	A	20010831	NZ 1998-337131		19980206
MX 9907290	A	20000531	MX 1999-7290		19990806
NZ 507275	A	20011130	NZ 2000-507275		20001003
NZ 507276	A	20020201	NZ 2000-507276		20001003
AU 771024	B2	20040311	AU 2000-72261		20001214
AU 771434	B2	20040325	AU 2000-72260		20001214
PRIORITY APPLN. INFO.:			US 1997-796334	A	19970207
			US 1997-796335	A	19970207
			US 1997-796336	A	19970207
			US 1997-796337	A	19970207
			US 1997-796338	A	19970207
			US 1997-796339	A	19970207
			US 1997-796340	A	19970207
			US 1997-796341	A	19970207
			US 1997-797100	A	19970207
			US 1997-797813	A	19970207
			US 1997-797816	A	19970207
			US 1997-797817	A	19970207
			US 1997-797820	A	19970207
			AU 1998-62756	A3	19980206
			CA 1998-2279331	A3	19980206
			EP 1998-905042	A3	19980206
			EP 1999-117292	A3	19980206
			JP 1998-535034	A3	19980206
			NZ 1998-337131	A1	19980206
			WO 1998-US2619	W	19980206

AB Carrier compds. and compns. therewith which are useful in the **delivery** of **active agents** are provided.
Methods of administration and preparation are provided as well. Standard methods
of preparation are mentioned for the 193 carrier compds. listed, which primarily are N-(fatty acid) benzamide derivs. Examples are listed for the **delivery** of parathyroid hormone, recombinant human growth hormone, interferon and the evaluation of heparin in rats.

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 19 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:414634 HCAPLUS
DOCUMENT NUMBER: 129:72224
TITLE: Oral drug **delivery** compositions and methods
INVENTOR(S): **Milstein, Sam J.**; Barantsevitch, Evgueni N.; **Sarubbi, Donald J.**; **Leone-Bay, Andrea**; Paton, Duncan R.
PATENT ASSIGNEE(S): Emisphere Technologies, Inc., USA
SOURCE: U.S., 40 pp., Cont.-in-part of U.S. 5,451,410.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 30
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

US 5766633	A	19980616	US 1995-537888	19951023	
US 5451410	A	19950919	US 1993-51019	19930422	
US 5792451	A	19980811	US 1994-205511	19940302	
AU 771024	B2	20040311	AU 2000-72261	20001214	
AU 771434	B2	20040325	AU 2000-72260	20001214	
PRIORITY APPLN. INFO.:			US 1993-51019	A2	19930422
			US 1994-205511	A2	19940302
			WO 1994-US4560	W	19940422
			AU 1998-62756	A3	19980206

OTHER SOURCE(S): MARPAT 129:72224

AB The present invention relates to an oral drug **delivery** system, and in particular to modified amino acids and modified amino acid derivs. for use as a **delivery** system of sensitive agents such as bioactive peptides. The modified amino acids and derivs. can form non-covalent mixts. with active biol. agents and in an alternate embodiment can releasably carry **active agents**. Modified amino acids can also form drug containing microspheres. These mixts. are suitable for oral administration of biol. **active agents** to animals. Methods for the preparation of such amino acids are also disclosed. In a test tube 568 mg acetyl phenylalanine aldehyde, 132 mg carbomethoxyphenylalanylleucine, and 100 mg N-acetyl-Phe-Leu-Leu-Arg aldehyde were added to 2.9 mL of 15 % ethanol. The solution was stirred and NaOH was added to raise the pH to 7.2 and water was added to bring the total volume to 4 mL. Calcitonin 6 μg was added to the solution to obtain an oral solution

REFERENCE COUNT: 311 THERE ARE 311 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 20 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:402289 HCAPLUS
DOCUMENT NUMBER: 129:86002
TITLE: **Active agent** transport systems
INVENTOR(S): **Milstein, Sam J.**; Barantsevitch, Evgueni; **Leone-Bay, Andrea**; Wang, Nai Fang; **Sarubbi, Donald J.**; Santiago, Noemi B.
PATENT ASSIGNEE(S): Emisphere Technologies, Inc., USA
SOURCE: PCT Int. Appl., 134 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 30
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9825589	A1	19980618	WO 1997-US23545	19971209
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 6099856	A	20000808	US 1996-763183	19961210
AU 9855322	A1	19980703	AU 1998-55322	19971209
AU 771024	B2	20040311	AU 2000-72261	20001214
AU 771434	B2	20040325	AU 2000-72260	20001214
PRIORITY APPLN. INFO.:			US 1996-763183 A	19961210

US 1992-898909	B2	19920615
US 1992-920346	A2	19920727
US 1993-51019	A2	19930422
US 1993-76803	A2	19930614
US 1993-143571	B2	19931026
US 1993-168776	A2	19931216
US 1994-205511	A2	19940302
US 1994-231622	A2	19940422
US 1994-231623	A2	19940422
WO 1994-US4560	A2	19940422
US 1994-315200	A2	19940929
US 1994-316404	A2	19940930
US 1994-328932	A2	19941025
WO 1997-US23545	W	19971209
AU 1998-62756	A3	19980206

OTHER SOURCE(S): MARPAT 129:86002

AB Methods for transporting a biol. **active agent** across a cellular membrane or a lipid bilayer. A first method includes the steps of: (a) providing a biol. **active agent** which can exist in a native conformational state, a denatured conformational state, and an intermediate conformational state which is reversible to the native state and which is conformationally between the native and denatured states; (b) exposing the biol. **active agent** to a complexing perturbant to reversibly transform the biol. **active agent** to the intermediate state and to form a transportable supramol. complex; and (c) exposing the membrane or bilayer to the supramol. complex, to transport the biol. **active agent** across the membrane or bilayer. The perturbant has a mol. weight between about 150 and about 600 daltons, and contains at least one hydrophilic moiety and at least one hydrophobic moiety. The supramol. complex comprises the perturbant non-covalently bound or complexed with the biol. **active agent.** In the present invention, the biol. **active agent** does not form a microsphere after interacting with the perturbant. A method for preparing an orally administrable biol. **active agent** comprising steps (a) and (b) above is also provided as are oral **delivery** compns. Addnl., mimetics and methods for preparing mimetics are contemplated.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 21 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1997:672238 HCAPLUS

DOCUMENT NUMBER: 127:322800

TITLE: Modified amino acids for drug **delivery**

INVENTOR(S): **Leone-Bay, Andrea**

PATENT ASSIGNEE(S): Emishphere Technologies, Inc., USA; Leone-Bay, Andrea

SOURCE: PCT Int. Appl., 64 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 30

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9736480	A1	19971009	WO 1997-US5128	19970318

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN,

YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

US 6090958	A	20000718	US 1997-797816		19970207
AU 9725956	A1	19971022	AU 1997-25956		19970318
AU 771024	B2	20040311	AU 2000-72261		20001214
AU 771434	B2	20040325	AU 2000-72260		20001214
PRIORITY APPLN. INFO.:			US 1996-17902	A1	19960329
			US 1996-17902P	P	19960329
			WO 1997-US5128	A2	19970318
			AU 1998-62756	A3	19980206

OTHER SOURCE(S): MARPAT 127:322800

AB Modified amino acid compds. useful in the **delivery** of **active agents** are provided. E.g., 2HOC6H4CONH(CH2)7CO2H was prepared from 8-aminocaprylic acid and O-acetylsalicyloyl chloride. Also examples were give of a nol. of **delivery** agents enhancement of recombinant human growth hormone bioavailability administered s.c. in rats.

L25 ANSWER 22 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:594748 HCAPLUS
DOCUMENT NUMBER: 127:248424
TITLE: Preparation of small oligopeptides as agents for oral drug **delivery**
INVENTOR(S): **Milstein, Sam J.**
PATENT ASSIGNEE(S): Emisphere Technologies, Inc., USA; Milstein, Sam J.
SOURCE: PCT Int. Appl., 143 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9731938	A1	19970904	WO 1997-US4051	19970228
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2247048	AA	19970904	CA 1997-2247048	19970228
AU 9724209	A1	19970916	AU 1997-24209	19970228
EP 883629	A1	19981216	EP 1997-919879	19970228
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE, FI				
PRIORITY APPLN. INFO.:			US 1996-12573P	P 19960229
			WO 1997-US4051	W 19970228

OTHER SOURCE(S): MARPAT 127:248424

AB The present invention relates to small oligopeptides pGlu(X)n and Pro(X)n (X = amino acid residue; n = 1 to about 10) and compns. prepared from them. Theses compns. comprising an oligopeptide, and an **active agent** are useful in the **delivery** of a cargo to a target, and particularly in the oral **delivery** of biol. or chemical **active agents.** Methods for the preparation and for the administration of such compns. are also disclosed. Thus,pyroglutamic acid peptides H-pGlu-Glu(Phe-OH)-OH, H-pGlu-Glu(Phe-OH)-Phe-OH, and

H-pGlu-Glu-Phe-Tyr-OH, prepd, by standard solution coupling methods, showed heparin binding affinity parameters Kd = 1.42 + 10-4, 1.46 + 10-4, and 1.89 + 10-4, resp.

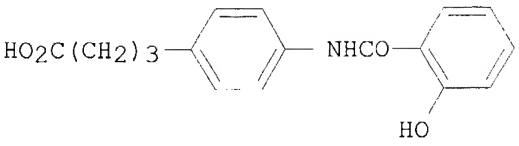
L25 ANSWER 23 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:527636 HCAPLUS
DOCUMENT NUMBER: 127:152958
TITLE: Modified amino acid carriers, their preparation, and compositions containing them for **delivering active agents**
INVENTOR(S): **Leone-Bay, Andrea**; Paton, Duncan R.; **Ho, Koc-Kan**; DeMorin, Frenel
PATENT ASSIGNEE(S): Emisphere Technologies, Inc., USA
SOURCE: U.S., 22 pp., Cont.-in-part of U.S. Ser. No. 231,622.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 30
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5643957	A	19970701	US 1994-335148	19941025
US 5451410	A	19950919	US 1993-51019	19930422
US 5792451	A	19980811	US 1994-205511	19940302
US 5629020	A	19970513	US 1994-231622	19940422
CA 2203033	AA	19960502	CA 1995-2203033	19951016
WO 9612473	A1	19960502	WO 1995-US13527	19951016
W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9539633	A1	19960515	AU 1995-39633	19951016
AU 711887	B2	19991021		
EP 783299	A1	19970716	EP 1995-937558	19951016
EP 783299	B1	20030910		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
BR 9510168	A	19971014	BR 1995-10168	19951016
HU 77759	A2	19980728	HU 1998-903	19951016
JP 10507762	T2	19980728	JP 1995-514062	19951016
AT 249422	E	20030915	AT 1995-937558	19951016
ES 2207655	T3	20040601	ES 1995-937558	19951016
US 5955503	A	19990921	US 1997-795833	19970206
US 6100298	A	20000808	US 1997-795837	19970206
NO 9701889	A	19970623	NO 1997-1889	19970424
FI 9701776	A	19970425	FI 1997-1776	19970425
US 2001003001	A1	20010607	US 2000-730156	20001205
AU 771024	B2	20040311	AU 2000-72261	20001214
AU 771434	B2	20040325	AU 2000-72260	20001214
US 2002120009	A1	20020829	US 2002-90012	20020221
US 6663887	B2	20031216		
US 2004068013	A1	20040408	US 2003-677906	20031001

PRIORITY APPLN. INFO.:
US 1993-51019 A2 19930422
US 1994-205511 A2 19940302
US 1994-231622 A2 19940422
WO 1994-US4560 A2 19940422
US 1994-335148 A 19941025

WO 1995-US13527	W	19951016
US 1997-795837	A1	19970206
AU 1998-62756	A3	19980206
US 1999-346970	A1	19990702
US 2000-730156	A1	20001205
US 2002-90012	A1	20020221

OTHER SOURCE(S): MARPAT 127:152958
GI



I

AB Modified amino acid compds. useful in the **delivery** of **active agents** (peptides, carbohydrates, antigens, monoclonal antibodies, hormones, pesticides, etc.) are provided. Methods of administration and preparation are also provided. The effect of a composition containing e.g. interferon-α2 and e.g. I (preparation given) on the serum interferon level was determined

L25 ANSWER 24 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:119253 HCAPLUS
DOCUMENT NUMBER: 126:135457
TITLE: Microspheres containing fragrances and flavorants
INVENTOR(S): **Milstein, Sam J.**
PATENT ASSIGNEE(S): Emisphere Technologies, Inc., USA; Milstein, Sam J.
SOURCE: PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9640070	A1	19961219	WO 1996-US10183	19960606
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA				
US 5824345	A	19981020	US 1995-484293	19950607
CA 2219035	AA	19961219	CA 1996-2219035	19960606
AU 9662765	A1	19961230	AU 1996-62765	19960606
EP 831784	A1	19980401	EP 1996-921566	19960606
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 11507916	T2	19990713	JP 1996-502232	19960606

PRIORITY APPLN. INFO.: US 1995-484293 A 19950607
WO 1996-US10183 W 19960606

AB Compns. useful in the **delivery** of fragrances and flavorant

active agents, and particularly vaporous fragrances and flavorants, are provided. These compns. include a microsphere which includes: (a) the **active agent**; and (b) (1) a proteinoid, (2) a modified hydrolyzed vegetable protein wherein the protein is modified with an amino **reactive agent**, or (3) a combination thereof. Clove oil/proteinoid microspheres were prepared by combing a mixture of 0.1% clove oil in 10% soluble proteinoid (Glu-Asp-Tyr-Phe) with an equal volume of 1.7 N citric acid and gum to prepare microspheres of clove oil/proteinoid microspheres.

L25 ANSWER 25 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:87 HCAPLUS
DOCUMENT NUMBER: 126:31174
TITLE: Preparation of modified amino acid compounds for **delivering active agents**
INVENTOR(S): **Leone-Bay, Andrea; Ho, Koc-Kan; Sarubbi, Donald J.; Milstein, Sam J.** ; Press, Jeffery Bruce
PATENT ASSIGNEE(S): Emisphere Technologies, Inc., USA; Leone-Bay, Andrea; Ho, Koc-Kan; Sarubbi, Donald, J.; Milstein, Sam, J.; Press, Jeffery, Bruce
SOURCE: PCT Int. Appl., 86 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 30
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9630036	A1	19961003	WO 1996-US4580	19960401
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA				
US 5650386	A	19970722	US 1995-414654	19950331
CA 2214323	AA	19961003	CA 1996-2214323	19960401
AU 9656629	A1	19961016	AU 1996-56629	19960401
AU 712222	B2	19991104		
EP 817643	A1	19980114	EP 1996-913778	19960401
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI				
BR 9604880	A	19980519	BR 1996-4880	19960401
JP 2002506418	T2	20020226	JP 1996-529751	19960401
RU 2203268	C2	20030427	RU 1997-118224	19960401
JP 2003313157	A2	20031106	JP 2003-140962	19960401
US 5965121	A	19991012	US 1997-798023	19970206
US 5989539	A	19991123	US 1997-798032	19970206
US 6001347	A	19991214	US 1997-798031	19970206
FI 9703828	A	19970929	FI 1997-3828	19970929
NO 9704495	A	19971128	NO 1997-4495	19970929
US 2001023240	A1	20010920	US 1999-305506	19990505
US 6428780	B2	20020806		
US 6346242	B1	20020212	US 2000-499958	20000208
AU 771024	B2	20040311	AU 2000-72261	20001214
AU 771434	B2	20040325	AU 2000-72260	20001214
US 2003045579	A1	20030306	US 2001-38426	20011019
US 6623731	B2	20030923		

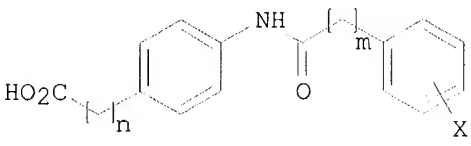
US 2003078302	A1	20030424	US 2002-142009	20020508
US 6699467	B2	20040302		
US 2004110839	A1	20040610	US 2003-623142	20030718

PRIORITY APPLN. INFO.:

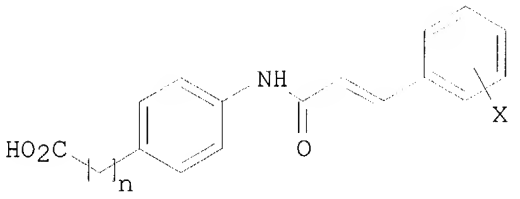
US 1995-414654	A2	19950331
US 1995-3111P	P	19950901
US 1996-17902P	P	19960329
JP 1996-529751	A3	19960401
WO 1996-US4580	W	19960401
US 1997-798031	A1	19970206
AU 1998-62756	A3	19980206
US 1999-305506	A1	19990505
US 2000-499958	A1	20000208
US 2001-38426	A1	20011019

OTHER SOURCE(S): MARPAT 126:31174

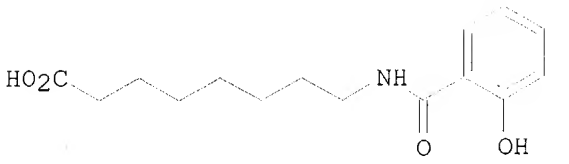
GI



I



II



III

AB Modified amino acid compds. [I (n = 0-3; m = 0-4; X = H, halo, OH, etc.), II (n = 0-3; X = 2-F, 3-MeO, 4-Me, etc.), etc.], useful in the **delivery** of **active agents** such as, e.g., human growth hormone, interferon, heparin, calcitonin, parathyroid hormone, were prepared Thus, reaction of 8-aminocaprylic acid with O-acetylsalicyloyl chloride in the presence of 2M aqueous NaOH afforded 57% III which was mixed with recombinant growth hormone (rhGH) in a phosphate buffer solution at pH 7-8 and administered orally to rats at 25 mg/kg of carrier and at 1 mg/kg of rhGH. The mean peak serum level of compound III was 60.92 ng/mL as compared to < 10 ng/mL for control.

L25 ANSWER 26 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1996:761910 HCAPLUS
DOCUMENT NUMBER: 126:37109

TITLE: Diamide-dicarboxylic acid microspheres
INVENTOR(S): **Milstein, Sam J.**
PATENT ASSIGNEE(S): Emisphere Technologies, Inc., USA; Milstein, Sam, J.
SOURCE: PCT Int. Appl., 78 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9633699	A1	19961031	WO 1996-US6502	19960429
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN				
US 5820881	A	19981013	US 1995-430491	19950428
CA 2219454	AA	19961031	CA 1996-2219454	19960429
AU 9657340	A1	19961118	AU 1996-57340	19960429
GB 2314508	A1	19980107	GB 1997-22756	19960429
GB 2314508	B2	19990616		

PRIORITY APPLN. INFO.: US 1995-430491 19950428
WO 1996-US6502 19960429

AB Diamide-dicarboxylic acid microspheres are provided. The diamide-dicarboxylic acids may be combined with **active agent**(s). The resultant composition may be in microsphere form. Also disclosed are methods for administering the microsphere and/or composition that includes the **active agent**. The microsphere, with or without **active agent**, may be prepared by (A) solubilizing, in a solvent, at least one diamide-dicarboxylic acid, to yield a first solution; and (B) contacting the first solution with a precipitator solution in which the diamide-carboxylic acid is insol. and optionally with an **active agent**. E.g., bis(Nσ-amido-L-phenylalanine) malonate was prepared and used to prepare microspheres.

L25 ANSWER 27 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1996:494675 HCAPLUS
DOCUMENT NUMBER: 125:151187
TITLE: Modified hydrolyzed vegetable protein microspheres and methods for preparation and use
INVENTOR(S): **Milstein, Sam J.**; Barantsevitch, Evgueni
PATENT ASSIGNEE(S): Emisphere Technologies, Inc., USA
SOURCE: U.S., 14 pp., Cont.-in-part of U.S. 5,401,516.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5540939	A	19960730	US 1994-233281	19940425
US 5401516	A	19950328	US 1993-51739	19930422

PRIORITY APPLN. INFO.: US 1992-995508 19921221
US 1993-51739 19930422

AB Modified hydrolyzed vegetable protein microspheres and methods for their

preparation and use as oral **delivery** systems for pharmaceutical agents, are described. A solution of soya proteins was treated with benzenesulfonyl chloride. An aqueous solution containing heparin, gum acacia, and citric acid was mixed with an aqueous solution containing heparin to give microspheres.

L25 ANSWER 28 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1996:434961 HCAPLUS
DOCUMENT NUMBER: 125:76328
TITLE: **Active agent** transport systems using perturbants to convert **active agent** to state between native and denatured states
INVENTOR(S): **Milstein, Sam J.**; Barantsevitch, Evgueni; **Leone-Bay, Andrea**; Wang, Nai Fang; **Sarubbi, Donald J.**; Santiago, Noemi B.
PATENT ASSIGNEE(S): Emisphere Technologies, Inc., USA
SOURCE: PCT Int. Appl., 119 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 30
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9612475	A1	19960502	WO 1995-US14598	19951024
W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5714167	A	19980203	US 1994-328932	19941025
CA 2202300	AA	19960502	CA 1995-2202300	19951024
AU 9641524	A1	19960515	AU 1996-41524	19951024
EP 781124	A1	19970702	EP 1995-939863	19951024
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 10509433	T2	19980914	JP 1995-514159	19951024
AU 771024	B2	20040311	AU 2000-72261	20001214
AU 771434	B2	20040325	AU 2000-72260	20001214

PRIORITY APPLN. INFO.:

US 1994-328932	A	19941025
US 1992-898909	B2	19920615
US 1992-920346	A2	19920727
US 1993-51019	A2	19930422
US 1993-76803	A2	19930614
US 1993-143571	B2	19931026
US 1993-168776	A2	19931216
US 1994-205511	A2	19940302
US 1994-231622	A2	19940422
US 1994-231623	A2	19940422
US 1994-315200	A2	19940929
US 1994-316404	A2	19940930
WO 1995-US14598	W	19951024
AU 1998-62756	A3	19980206

OTHER SOURCE(S): MARPAT 125:76328
AB Methods are disclosed for transporting a biol. **active agent** across a cellular membrane or a lipid bilayer. A first

method includes the steps of: (a) providing a biol. **active agent** which can exist in a native conformational state, a denatured conformational state, and an intermediate conformational state which is reversible to the native state and which is conformationally between the native and denatured states; (b) exposing the biol. **active agent** to a complexing perturbant to reversibly transform the biol. **active agent** to the intermediate state and to form a transportable supramol. complex; and (c) exposing the membrane or bilayer to the supramol. complex, to transport the biol. **active agent** across the membrane or bilayer. The perturbant has a mol. weight between about 150 and about 600 daltons, and contains at least one hydrophilic moiety and at least one hydrophobic moiety. The supramol. complex comprises the perturbant noncovalently bound or complexed with the biol. **active agent**. In the present invention, the biol. **active agent** does not form a microsphere after interacting with the perturbant. A method for preparing an orally administrable biol. **active agent** comprising steps (a) and (b) above is also provided as are oral **delivery** compns. Addnl., mimetics and methods for preparing mimetics are contemplated. The methods and compns. of the invention facilitate the **delivery** of an **active agent** to a target, e.g. the **delivery** of a pharmaceutical through an adverse environment to a particular location in the body. The biol. **active agent** may be e.g. a carbohydrate, mucopolysaccharide, lipid, pesticide, or peptide, e.g. human or bovine growth hormone, an interferon, insulin, an antigen, a monoclonal antibody, cromolyn sodium, vancomycin, heparin, etc. The perturbant may be e.g. a proteinoid, carboxylic acid, or acylated amino acid or poly(amino acid). The perturbant may also be a pH-changing agent, an ionic strength-changing agent, or guanidine-HCl.

L25 ANSWER 29 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1996:425385 HCAPLUS
DOCUMENT NUMBER: 125:96071
TITLE: Modified amino acids as absorption enhancers for **delivering active agents**
INVENTOR(S): **Leone-Bay, Andrea**; Paton, Duncan R.; Ho, Kok-Kan; Demorin, Frenel
PATENT ASSIGNEE(S): Emisphere Technologies, Inc., USA
SOURCE: PCT Int. Appl., 57 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 30
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9612473	A1	19960502	WO 1995-US13527	19951016
W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5643957	A	19970701	US 1994-335148	19941025
AU 9539633	A1	19960515	AU 1995-39633	19951016
AU 711887	B2	19991021		
EP 783299	A1	19970716	EP 1995-937558	19951016
EP 783299	B1	20030910		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE

BR 9510168	A	19971014	BR 1995-10168	19951016	
JP 10507762	T2	19980728	JP 1995-514062	19951016	
AT 249422	E	20030915	AT 1995-937558	19951016	
NO 9701889	A	19970623	NO 1997-1889	19970424	
FI 9701776	A	19970425	FI 1997-1776	19970425	
AU 771024	B2	20040311	AU 2000-72261	20001214	
AU 771434	B2	20040325	AU 2000-72260	20001214	

PRIORITY APPLN. INFO.:

US 1994-335148	A	19941025
US 1993-51019	A2	19930422
US 1994-205511	A2	19940302
US 1994-231622	A2	19940422
WO 1995-US13527	W	19951016
AU 1998-62756	A3	19980206

AB Modified amino acid compds. as absorption enhancers are useful in the **delivery** of **active agents.** These compound are used as carriers to facilitate the **delivery** of a cargo to a target. Thus, 47.00 g acetylsalicyloyl chloride was added to a mixture of 50.00 g 4-(4-aminophenyl)butyric acid in 300 mL of 2M aqueous sodium hydroxide and the reaction was stirred at 25° for 2 h, then it was acidified with aqueous HCl to obtain a precipitate which was separated and washed to give 31.89 g 4-(2-hydroxyphenylcarbonylamino)p-phenylbutanoic acid (I). I was mixed with interferon α-2 (II) in Tris-HCl buffer pH = 7-8 and was orally administered to rats at a rate of 300 mg I/kg and 1000 μg II/kg. The mean peak serum level of II was 8213 as compared to 688 ng/mL for controls.

L25 ANSWER 30 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:	1996:417849 HCAPLUS
DOCUMENT NUMBER:	125:67703
TITLE:	Carbon-substituted diketopiperazine **delivery** systems
INVENTOR(S):	**Milstein, Sam J.**
PATENT ASSIGNEE(S):	Emisphere Technologies, Inc., USA
SOURCE:	PCT Int. Appl., 25 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	30

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9610396	A1	19960411	WO 1995-US12887	19950928
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 6331318	B1	20011218	US 1994-316404	19940930
AU 9641292	A1	19960426	AU 1996-41292	19950928
AU 771024	B2	20040311	AU 2000-72261	20001214
AU 771434	B2	20040325	AU 2000-72260	20001214
US 2002028250	A1	20020307	US 2001-929530	20010813
US 6395774	B2	20020528		
US 2002155993	A1	20021024	US 2002-125836	20020419
US 6663898	B2	20031216		

US 2003198658 A1 20031023 US 2003-443713 20030521
PRIORITY APPLN. INFO.: US 1994-316404 A 19940930
WO 1995-US12887 W 19950928
AU 1998-62756 A3 19980206
US 2001-929530 A1 20010813
US 2002-125836 A1 20020419
OTHER SOURCE(S): MARPAT 125:67703
AB Compns. useful in the **delivery** of **active agents** are provided. These **delivery** compns. include (a) an **active agent**; and (b) a carrier of at least one mono-C-substituted or di-C-substituted diketopiperazine. E.g., the diketopiperazine derivative of glutamic acid was prepared and diketopiperazine derivs. microspheres were prepared cong. encapsulated salmon calcitonin.

L25 ANSWER 31 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1996:401663 HCAPLUS
DOCUMENT NUMBER: 125:67698
TITLE: Diketopiperazine-based drug **delivery** systems
INVENTOR(S): **Milstein, Sam J.**
PATENT ASSIGNEE(S): Emisphere Technologies, Inc., USA
SOURCE: PCT Int. Appl., 51 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 30
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9609813	A1	19960404	WO 1995-US12888	19950928
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5693338	A	19971202	US 1994-315200	19940929
AU 9641293	A1	19960419	AU 1996-41293	19950928
US 5976569	A	19991102	US 1997-841101	19970429
AU 771024	B2	20040311	AU 2000-72261	20001214
AU 771434	B2	20040325	AU 2000-72260	20001214

PRIORITY APPLN. INFO.: US 1994-315200 A 19940929
WO 1995-US12888 W 19950928
AU 1998-62756 A3 19980206

AB Compns. useful in the **delivery** of **active agents** are provided. These **delivery** compns. include: (a) an **active agent**; and either (b)(1) a carrier of (i) at least one amino acid and (ii) at least one diketopiperazine or (b)(2) at least one mono-N-substituted, di-N-substituted, or unsubstituted diketopiperazine. Methods for preparing these compns. and administering these compns. are also provided. Thus, 6 fasted rats were anesthetized. The rats were administered by oral gavage a calcitonin/L-Phe-(diketo-L-Asp)-L-Phe composition containing 1.5 μg of calcitonin/mL. Each rat was administered a dosage of 10 μg/kg. The amount of diketopiperazine in the dosage was 300 mg/kg. Blood samples were collected serially from the caudal artery, and serum calcium was determined The carriers of the present invention facilitated the reduction of serum calcitonin and, therefore, the oral **delivery** of calcitonin.

L25 ANSWER 32 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1995:1000101 HCAPLUS
DOCUMENT NUMBER: 124:66617
TITLE: Acids and acid salts and their use in **delivery** systems
INVENTOR(S): **Leone-Bay, Andrea**; Santiago, Noemi B.
PATENT ASSIGNEE(S): Emisphere Technologies, Inc., USA
SOURCE: PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 30
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9528920	A1	19951102	WO 1995-US5110	19950421
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT, UA				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5541155	A	19960730	US 1994-231623	19940422
AU 9523644	A1	19951116	AU 1995-23644	19950421
ZA 9503246	A	19960112	ZA 1995-3246	19950421
AU 771024	B2	20040311	AU 2000-72261	20001214
AU 771434	B2	20040325	AU 2000-72260	20001214

PRIORITY APPLN. INFO.: US 1994-231623 A 19940422
WO 1995-US5110 W 19950421
AU 1998-62756 A3 19980206
OTHER SOURCE(S): MARPAT 124:66617
AB The present invention relates to a **delivery** system, and in particular to carboxylic acids for use as a **delivery** system, of sensitive agents such as bioactive peptides. The carboxylic acids and salts can form noncovalent mixts. with biol.-**active agents**. These mixts. are suitable for oral administration of biol. **active agents** to animals. An aqueous solution (pH 7.0-7.6) of cyclohexanepropionic acid sodium salt was mixed with calcitonin to have a final carrier concentration 200 mg/mL and calcitonin concentration
5 μg/mL; the composition was orally administered to rats and serum Ca levels were monitored to show improved bioavailability as compared to the control which did not contain Na cyclohexanepropionate.

L25 ANSWER 33 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1995:992845 HCAPLUS
DOCUMENT NUMBER: 124:37744
TITLE: Modified amino acids for drug **delivery**.
INVENTOR(S): **Leone-bay, Andrea**; Wang, Nai Fang
PATENT ASSIGNEE(S): Emisphere Technologies, Inc., USA
SOURCE: PCT Int. Appl., 53 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 30
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9528838	A1	19951102	WO 1995-US5112	19950421

W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

US 5629020	A	19970513	US 1994-231622	19940422
CA 2188467	AA	19951102	CA 1995-2188467	19950421
AU 9523963	A1	19951116	AU 1995-23963	19950421
EP 758843	A1	19970226	EP 1995-917157	19950421
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 09512279	T2	19971209	JP 1995-527834	19950421
US 6180140	B1	20010130	US 1995-460265	19950602
US 5935601	A	19990810	US 1996-732404	19961022
AU 771024	B2	20040311	AU 2000-72261	20001214
AU 771434	B2	20040325	AU 2000-72260	20001214

PRIORITY APPLN. INFO.: US 1994-231622 A 19940422
WO 1995-US5112 W 19950421
AU 1998-62756 A3 19980206

OTHER SOURCE(S): MARPAT 124:37744

AB Th invention relates to an oral **delivery** system, and in particular to modified amino acids or peptides, for **delivery** sensitive agents such as bioactive peptides. The modified amino acids or peptides can form no-covalent mixts. or microspheres with active biol. agents. These mixts. or microspheres are suitable for oral administration of biol. **active agents** to animals. Methods for the preparation of such amino acids and peptides, for example N-cyclohexanoyl-L-tyrosine, are disclosed.

L25 ANSWER 34 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1995:951479 HCAPLUS
DOCUMENT NUMBER: 124:15498
TITLE: Modified amino acids for encapsulating **active agents**
INVENTOR(S): **Milstein, Sam J.**; Barantsetvich, Evgueni N.
PATENT ASSIGNEE(S): Emisphere Technologies, Inc., USA
SOURCE: U.S., 9 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 30
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5451410	A	19950919	US 1993-51019	19930422
US 5447728	A	19950905	US 1993-168776	19931216
CA 2160693	AA	19941027	CA 1994-2160693	19940422
ZA 9402804	A	19950104	ZA 1994-2804	19940422
EP 696208	A1	19960214	EP 1994-916578	19940422
EP 696208	B1	20010822		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 08509474	T2	19961008	JP 1994-523595	19940422
EP 1025840	A2	20000809	EP 2000-103527	19940422
EP 1025840	A3	20000830		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
EP 1077070	A2	20010221	EP 2000-118505	19940422
EP 1077070	A3	20010523		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				

AT	204467	E	20010915	AT 1994-916578	19940422
ES	2163444	T3	20020201	ES 1994-916578	19940422
US	5643957	A	19970701	US 1994-335148	19941025
US	5714167	A	19980203	US 1994-328932	19941025
US	5709861	A	19980120	US 1995-372208	19950113
US	5958457	A	19990928	US 1995-438644	19950510
US	5766633	A	19980616	US 1995-537888	19951023
US	5811127	A	19980922	US 1996-635921	19960424
US	6099856	A	20000808	US 1996-763183	19961210
US	5955503	A	19990921	US 1997-795833	19970206
US	6100298	A	20000808	US 1997-795837	19970206
US	6221367	B1	20010424	US 1997-939939	19970929
US	6071538	A	20000606	US 1997-940056	19970930
US	6245359	B1	20010612	US 1997-941616	19970930
US	6348207	B1	20020219	US 1997-941609	19970930
US	2001003001	A1	20010607	US 2000-730156	20001205
AU	771024	B2	20040311	AU 2000-72261	20001214
AU	771434	B2	20040325	AU 2000-72260	20001214
US	2001039258	A1	20011108	US 2001-760307	20010111
US	2002001591	A1	20020103	US 2001-862013	20010521
US	6610329	B2	20030826		
US	2002052422	A1	20020502	US 2001-862063	20010521
US	6461643	B2	20021008		
US	2002120009	A1	20020829	US 2002-90012	20020221
US	6663887	B2	20031216		
US	2003012817	A1	20030116	US 2002-225104	20020820
US	2003133953	A1	20030717	US 2002-255237	20020925
US	2004062773	A1	20040401	US 2003-600386	20030619
US	2004068013	A1	20040408	US 2003-677906	20031001

PRIORITY APPLN. INFO.:

US	1992-898909	B2	19920615
US	1992-920346	A2	19920727
US	1993-51019	A2	19930422
US	1993-76803	A2	19930614
US	1993-143571	B2	19931026
US	1993-168776	A2	19931216
US	1994-205511	A	19940302
EP	1994-916578	A3	19940422
US	1994-231622	A2	19940422
US	1994-231623	A2	19940422
WO	1994-US4560	W	19940422
US	1994-315200	A2	19940929
US	1994-316404	A2	19940930
WO	1994-US12333	W	19941024
US	1994-328932	A2	19941025
US	1994-335147	B2	19941025
US	1994-335148	A3	19941025
US	1995-438644	A1	19950510
US	1996-17902P	P	19960329
US	1996-763183	A2	19961210
US	1997-795837	A1	19970206
US	1997-820694	A2	19970318
US	1997-939939	A1	19970929
AU	1998-62756	A3	19980206
US	1999-346970	A1	19990702
US	1999-346971	B1	19990702
US	1999-420200	A1	19991018
US	2000-730156	A1	20001205
US	2001-862013	A1	20010521
US	2001-862063	A1	20010521
US	2002-90012	A1	20020221

AB Modified amino acids and methods for their preparation and use as oral **delivery** systems for pharmaceutical agents are described. The modified amino acids are preparable by reacting single amino acid or mixts. of two or more kinds of amino acids with an amino modifying agent such as benzenesulfonyl chloride, benzoyl chloride, and hippuryl chloride. The modified amino acids form encapsulating microspheres in the presence of the **active agent** under sphere-forming conditions. Alternatively, the modified amino acids may be used as a carrier by simply mixing the amino acids with the **active agent**. The modified amino acids are particularly useful in **delivering** peptides, e.g. insulin or calmodulin, or other agents which are sensitive to the denaturing conditions of the gastrointestinal tract. A mixture of 16 amino acids was treated with benzenesulfonyl chloride and the product dissolved in distilled water was mixed with a salmon calcitonin solution at 40° to obtain a microsphere suspension, suitable for oral administration.

L25 ANSWER 35 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1995:846860 HCAPLUS
DOCUMENT NUMBER: 123:266168
TITLE: Modified amino acids for oral **delivery** of sensitive **bioactive agents**
INVENTOR(S): **Milstein, Sam J.**; Barantsevitch, Evgueni
PATENT ASSIGNEE(S): Emisphere Technologies, Inc., USA
SOURCE: U.S., 12 pp. Cont.-in-part of U.S. Ser. No. 51,019.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 30
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5447728	A	19950905	US 1993-168776	19931216
US 5443841	A	19950822	US 1992-920346	19920727
US 5451410	A	19950919	US 1993-51019	19930422
US 5578323	A	19961126	US 1993-76803	19930614
CA 2174961	AA	19950504	CA 1994-2174961	19941024
WO 9511690	A1	19950504	WO 1994-US12333	19941024
W: AM, AT, AU, BB, BG, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN				
AU 9480936	A1	19950522	AU 1994-80936	19941024
ZA 9408342	A	19950622	ZA 1994-8342	19941024
EP 726771	A1	19960821	EP 1994-932077	19941024
EP 726771	B1	20020123		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 09504300	T2	19970428	JP 1994-512827	19941024
EP 1072255	A2	20010131	EP 2000-117452	19941024
EP 1072255	A3	20010926		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
AT 212186	E	20020215	AT 1994-932077	19941024
ES 2171471	T3	20020916	ES 1994-932077	19941024
US 5714167	A	19980203	US 1994-328932	19941025
US 5811127	A	19980922	US 1996-635921	19960424
US 6099856	A	20000808	US 1996-763183	19961210
US 6221367	B1	20010424	US 1997-939939	19970929
US 6071538	A	20000606	US 1997-940056	19970930
US 6245359	B1	20010612	US 1997-941616	19970930

US 6348207	B1	20020219	US 1997-941609	19970930
AU 771024	B2	20040311	AU 2000-72261	20001214
AU 771434	B2	20040325	AU 2000-72260	20001214
US 2001039258	A1	20011108	US 2001-760307	20010111
US 2003133953	A1	20030717	US 2002-255237	20020925

PRIORITY APPLN. INFO.:

US 1992-898909	B2	19920615
US 1992-920346	A2	19920727
US 1993-51019	A2	19930422
US 1993-76803	A2	19930614
US 1993-143571	B2	19931026
US 1993-168776	A	19931216
US 1994-205511	A2	19940302
US 1994-231622	A2	19940422
US 1994-231623	A2	19940422
WO 1994-US4560	A2	19940422
US 1994-315200	A2	19940929
US 1994-316404	A2	19940930
EP 1994-932077	A3	19941024
WO 1994-US12333	W	19941024
US 1994-328932	A2	19941025
US 1996-17902P	P	19960329
US 1996-763183	A2	19961210
US 1997-820694	A2	19970318
US 1997-939939	A1	19970929
AU 1998-62756	A3	19980206
US 1999-420200	A1	19991018

AB Modified amino acids and methods for their preparation and use as oral **delivery** systems for pharmaceutical agents are described. The modified amino acids are preparable by reacting single amino acids or mixts. of two or more kinds of amino acids with an amino modifying agent such as benzene sulfonyl chloride, benzoyl chloride, and hippuryl chloride. The modified amino acids form encapsulating microspheres in the presence of the **active agent** under sphere-forming conditions. Alternatively, the modified amino acids may be used as a carrier by simply mixing the amino acids with the **active agent**. The modified amino acids are particularly useful in **delivering** peptides or other agents which are sensitive to the denaturing conditions of the gastrointestinal tract. For example, an oral composition containing desferrioxamine (I) and salicyloyl phenylalanine was administered to monkeys to evaluate iron clearance efficacy; oral administration of I in the absence of the modified amino acid induced little clearance of iron, in contrast, I prepared with the amino acid carrier induced a rapid secretion of iron in both urine and feces.

L25 ANSWER 36 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:	1995:532343 HCAPLUS
DOCUMENT NUMBER:	122:274108
TITLE:	Modified hydrolyzed vegetable protein microspheres and methods for preparation and use thereof
INVENTOR(S):	**Milstein, Sam J.**; Barantsevitch, Evgueni N.
PATENT ASSIGNEE(S):	Emisphere Technologies, Inc., USA
SOURCE:	U.S., 10 pp. Cont.-in-part of U.S. Ser. No. 995,508, abandoned. CODEN: USXXAM
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

US 5401516	A	19950328	US 1993-51739	19930422
WO 9414420	A1	19940707	WO 1993-US12700	19931221
W: AT, AU, BB, BG, BR, CA, CH, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, LV, MG, MN, MW, NL, NO, PL, RO, RU, SD, SE, UZ, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2151818	AA	19940707	CA 1993-2151818	19931221
AU 9460171	A1	19940719	AU 1994-60171	19931221
CN 1094611	A	19941109	CN 1993-119951	19931221
EP 674507	A1	19951004	EP 1994-906480	19931221
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 08507043	T2	19960730	JP 1993-515498	19931221
ZA 9309608	A	19940824	ZA 1993-9608	19931222
WO 9423702	A1	19941027	WO 1994-US4561	19940422
W: AT, AU, BB, BG, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KG, KP, KR, KZ, LK, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2160692	AA	19941027	CA 1994-2160692	19940422
AU 9466685	A1	19941108	AU 1994-66685	19940422
EP 696192	A1	19960214	EP 1994-915419	19940422
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 08509231	T2	19961001	JP 1994-523596	19940422
US 5540939	A	19960730	US 1994-233281	19940425
US 5972387	A	19991026	US 1994-342900	19941121

PRIORITY APPLN. INFO.:

US 1992-995508	19921221
US 1993-51739	19930422
WO 1993-US12700	19931221
WO 1994-US4561	19940422

AB Modified hydrolyzed vegetable protein microspheres and methods for their preparation and use as oral **delivery** systems for pharmaceutical agents are described. For example, an acid-hydrolyzed liquid soybean protein solution was reduced and extracted with methanol; the obtained soybean protein was dissolved in an aqueous solution of KOH while heating. Thereafter, benzenesulfonyl chloride was added to the mixture to obtain modified proteins, which were used to manufacture insulin-encapsulated microspheres. The insulin microspheres were orally administered to rats and the results showed that encapsulated insulin had a greater biol. effect, in contrast to unencapsulated insulin.

L25 ANSWER 37 OF 37 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1994:226961 HCAPLUS
DOCUMENT NUMBER: 120:226961
TITLE: Proteinoid carriers and methods for preparation and use thereof
INVENTOR(S): **Milstein, Sam J.**; Kantor, Martin L.
PATENT ASSIGNEE(S): Emisphere Technologies, Inc., USA
SOURCE: PCT Int. Appl., 104 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 30
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9325583	A2	19931223	WO 1993-US5723	19930615
WO 9325583	A3	19940804		

W: AT, AU, BG, BR, CA, CH, DE, DK, ES, FI, GB, HU, JP, LU, MG, MN, NL, NO, PL, RO, US
RW: AT, BE, CH, DE, DK, ES, FR, GB, IE, IT, LU, MC, NL, PT, SE

US 5443841	A	19950822	US 1992-920346	19920727	
US 5578323	A	19961126	US 1993-76803	19930614	
AU 9346356	A1	19940104	AU 1993-46356	19930615	
EP 642532	A1	19950315	EP 1993-916542	19930615	

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE

JP 07508004	T2	19950907	JP 1993-501793	19930615	
BR 9306678	A	19981208	BR 1993-6678	19930615	
NO 9404852	A	19950210	NO 1994-4852	19941214	
FI 9405912	A	19950215	FI 1994-5912	19941215	
AU 771024	B2	20040311	AU 2000-72261	20001214	
AU 771434	B2	20040325	AU 2000-72260	20001214	

PRIORITY APPLN. INFO.:

US 1992-898909	A	19920615
US 1992-920346	A	19920727
US 1993-76803	A	19930614
WO 1993-US5723	A	19930615
AU 1998-62756	A3	19980206

AB Proteinoid carriers are prepared from peptides having 2-20 amino acids and a mol. weight of 250-2400 daltons as a **delivery** system for a biol. **active agent**, a fragrance, a cosmetic agent, etc. The proteinoids are soluble within selected pH ranges in the gastrointestinal tract and display enhanced stability towards photolysis or decomposition over time. For example, a proteinoid carrier encapsulating murine IgG monoclonal antibody was prepared having final concentration of 50 mg/mL proteinoid prepared from a reaction mixture containing Glu, Asp, Tyr, and Phe at 1:1:1:1 mol ratio, the antibody 0.7 mg/mL, and gum arabic 0.5% in 0.85 N citric acid.